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(21) International Application Number: PCT/US00/08896 (22) International Filing Date: 3 April 2000 (03.04.00) (30) Priority Data: <table border="0"><tr><td>09/285,479</td><td>2 April 1999 (02.04.99)</td><td>US</td></tr><tr><td>09/466,396</td><td>17 December 1999 (17.12.99)</td><td>US</td></tr><tr><td>09/476,496</td><td>30 December 1999 (30.12.99)</td><td>US</td></tr><tr><td>09/480,884</td><td>10 January 2000 (10.01.00)</td><td>US</td></tr><tr><td>09/510,376</td><td>22 February 2000 (22.02.00)</td><td>US</td></tr></table> (71) Applicant (for all designated States except US): CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): WANG, Tongtong [US/US]; 8049 NE 28th Street, Medina, WA 98039 (US). FAN, Liquan [CN/US]; 14116 SE 46th Street, Bellevue, WA 98006 (US). (74) Agents: MAKI, David, J.; Seed Intellectual Property Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 (US) et al.		09/285,479	2 April 1999 (02.04.99)	US	09/466,396	17 December 1999 (17.12.99)	US	09/476,496	30 December 1999 (30.12.99)	US	09/480,884	10 January 2000 (10.01.00)	US	09/510,376	22 February 2000 (22.02.00)	US	(81) Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
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09/510,376	22 February 2000 (22.02.00)	US															
(54) Title: COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER (57) Abstract Compounds and methods for the treatment and diagnosis of lung cancer are provided. The inventive compounds include polypeptides containing at least a portion of a lung tumor protein. Vaccines and pharmaceutical compositions for immunotherapy of lung cancer comprising such polypeptides, or DNA molecules encoding such polypeptides, are also provided, together with DNA molecules for preparing the inventive polypeptides.																	

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COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER

TECHNICAL FIELD

5 The present invention relates generally to therapy and diagnosis of cancer, such as lung cancer. The invention is more specifically related to polypeptides comprising at least a portion of a lung tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of lung cancer, and for the
10 diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

 Lung cancer is the primary cause of cancer death among both men and women in the U.S., with an estimated 172,000 new cases being reported in 1994. The five-year survival rate among all lung cancer patients, regardless of the stage of disease
15 at diagnosis, is only 13%. This contrasts with a five-year survival rate of 46% among cases detected while the disease is still localized. However, only 16% of lung cancers are discovered before the disease has spread.

 Early detection is difficult since clinical symptoms are often not seen until the disease has reached an advanced stage. Currently, diagnosis is aided by the
20 use of chest x-rays, analysis of the type of cells contained in sputum and fiberoptic examination of the bronchial passages. Treatment regimens are determined by the type and stage of the cancer, and include surgery, radiation therapy and/or chemotherapy. In spite of considerable research into therapies for the disease, lung cancer remains difficult to treat.

25 Accordingly, there remains a need in the art for improved vaccines, treatment methods and diagnostic techniques for lung cancer.

SUMMARY OF THE INVENTION

 Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as lung cancer. In one aspect, the present

invention provides polypeptides comprising at least a portion of a lung tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises a sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347 and 349; (b) variants of a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347 and 349; and (c) complements of a sequence of (a) or (b). In specific embodiments, the polypeptides of the present invention comprise at least a portion of a tumor protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 152, 155, 156, 165, 166, 169, 170, 172, 174, 176, 226-252, 338-344 and 346, and variants thereof.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a lung tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a lung tumor protein; and (b) a physiologically acceptable carrier.

5 Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

10 Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above, and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

15 Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

20 Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

25 The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a lung tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

30 Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a lung tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Determined T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells determined from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a lung tumor protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be lung cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the

sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

5

SEQUENCE IDENTIFIERS

SEQ ID NO: 1 is the determined cDNA sequence for LST-S1-2

SEQ ID NO: 2 is the determined cDNA sequence for LST-S1-28

SEQ ID NO: 3 is the determined cDNA sequence for LST-S1-90

10 SEQ ID NO: 4 is the determined cDNA sequence for LST-S1-144

SEQ ID NO: 5 is the determined cDNA sequence for LST-S1-133

SEQ ID NO: 6 is the determined cDNA sequence for LST-S1-169

SEQ ID NO: 7 is the determined cDNA sequence for LST-S2-6

SEQ ID NO: 8 is the determined cDNA sequence for LST-S2-11

15 SEQ ID NO: 9 is the determined cDNA sequence for LST-S2-17

SEQ ID NO: 10 is the determined cDNA sequence for LST-S2-25

SEQ ID NO: 11 is the determined cDNA sequence for LST-S2-39

SEQ ID NO: 12 is a first determined cDNA sequence for LST-S2-43

SEQ ID NO: 13 is a second determined cDNA sequence for LST-S2-43

20 SEQ ID NO: 14 is the determined cDNA sequence for LST-S2-65

SEQ ID NO: 15 is the determined cDNA sequence for LST-S2-68

SEQ ID NO: 16 is the determined cDNA sequence for LST-S2-72

SEQ ID NO: 17 is the determined cDNA sequence for LST-S2-74

SEQ ID NO: 18 is the determined cDNA sequence for LST-S2-103

25 SEQ ID NO: 19 is the determined cDNA sequence for LST-S2-N1-1F

SEQ ID NO: 20 is the determined cDNA sequence for LST-S2-N1-2A

SEQ ID NO: 21 is the determined cDNA sequence for LST-S2-N1-4H

SEQ ID NO: 22 is the determined cDNA sequence for LST-S2-N1-5A

SEQ ID NO: 23 is the determined cDNA sequence for LST-S2-N1-6B

30 SEQ ID NO: 24 is the determined cDNA sequence for LST-S2-N1-7B

SEQ ID NO: 25 is the determined cDNA sequence for LST-S2-N1-7H

- SEQ ID NO: 26 is the determined cDNA sequence for LST-S2-N1-8A
SEQ ID NO: 27 is the determined cDNA sequence for LST-S2-N1-8D
SEQ ID NO: 28 is the determined cDNA sequence for LST-S2-N1-9A
SEQ ID NO: 29 is the determined cDNA sequence for LST-S2-N1-9E
5 SEQ ID NO: 30 is the determined cDNA sequence for LST-S2-N1-10A
SEQ ID NO: 31 is the determined cDNA sequence for LST-S2-N1-10G
SEQ ID NO: 32 is the determined cDNA sequence for LST-S2-N1-11A
SEQ ID NO: 33 is the determined cDNA sequence for LST-S2-N1-12C
SEQ ID NO: 34 is the determined cDNA sequence for LST-S2-N1-12E
10 SEQ ID NO: 35 is the determined cDNA sequence for LST-S2-B1-3D
SEQ ID NO: 36 is the determined cDNA sequence for LST-S2-B1-6C
SEQ ID NO: 37 is the determined cDNA sequence for LST-S2-B1-5D
SEQ ID NO: 38 is the determined cDNA sequence for LST-S2-B1-5F
SEQ ID NO: 39 is the determined cDNA sequence for LST-S2-B1-6G
15 SEQ ID NO: 40 is the determined cDNA sequence for LST-S2-B1-8A
SEQ ID NO: 41 is the determined cDNA sequence for LST-S2-B1-8D
SEQ ID NO: 42 is the determined cDNA sequence for LST-S2-B1-10A
SEQ ID NO: 43 is the determined cDNA sequence for LST-S2-B1-9B
SEQ ID NO: 44 is the determined cDNA sequence for LST-S2-B1-9F
20 SEQ ID NO: 45 is the determined cDNA sequence for LST-S2-B1-12D
SEQ ID NO: 46 is the determined cDNA sequence for LST-S2-I2-2B
SEQ ID NO: 47 is the determined cDNA sequence for LST-S2-I2-5F
SEQ ID NO: 48 is the determined cDNA sequence for LST-S2-I2-6B
SEQ ID NO: 49 is the determined cDNA sequence for LST-S2-I2-7F
25 SEQ ID NO: 50 is the determined cDNA sequence for LST-S2-I2-8G
SEQ ID NO: 51 is the determined cDNA sequence for LST-S2-I2-9E
SEQ ID NO: 52 is the determined cDNA sequence for LST-S2-I2-12B
SEQ ID NO: 53 is the determined cDNA sequence for LST-S2-H2-2C
SEQ ID NO: 54 is the determined cDNA sequence for LST-S2-H2-1G
30 SEQ ID NO: 55 is the determined cDNA sequence for LST-S2-H2-4G
SEQ ID NO: 56 is the determined cDNA sequence for LST-S2-H2-3H

- SEQ ID NO: 57 is the determined cDNA sequence for LST-S2-H2-5G
SEQ ID NO: 58 is the determined cDNA sequence for LST-S2-H2-9B
SEQ ID NO: 59 is the determined cDNA sequence for LST-S2-H2-10H
SEQ ID NO: 60 is the determined cDNA sequence for LST-S2-H2-12D
5 SEQ ID NO: 61 is the determined cDNA sequence for LST-S3-2
SEQ ID NO: 62 is the determined cDNA sequence for LST-S3-4
SEQ ID NO: 63 is the determined cDNA sequence for LST-S3-7
SEQ ID NO: 64 is the determined cDNA sequence for LST-S3-8
SEQ ID NO: 65 is the determined cDNA sequence for LST-S3-12
10 SEQ ID NO: 66 is the determined cDNA sequence for LST-S3-13
SEQ ID NO: 67 is the determined cDNA sequence for LST-S3-14
SEQ ID NO: 68 is the determined cDNA sequence for LST-S3-16
SEQ ID NO: 69 is the determined cDNA sequence for LST-S3-21
SEQ ID NO: 70 is the determined cDNA sequence for LST-S3-22
15 SEQ ID NO: 71 is the determined cDNA sequence for LST-S1-7
SEQ ID NO: 72 is the determined cDNA sequence for LST-S1-A-1E
SEQ ID NO: 73 is the determined cDNA sequence for LST-S1-A-1G
SEQ ID NO: 74 is the determined cDNA sequence for LST-S1-A-3E
SEQ ID NO: 75 is the determined cDNA sequence for LST-S1-A-4E
20 SEQ ID NO: 76 is the determined cDNA sequence for LST-S1-A-6D
SEQ ID NO: 77 is the determined cDNA sequence for LST-S1-A-8D
SEQ ID NO: 78 is the determined cDNA sequence for LST-S1-A-10A
SEQ ID NO: 79 is the determined cDNA sequence for LST-S1-A-10C
SEQ ID NO: 80 is the determined cDNA sequence for LST-S1-A-9D
25 SEQ ID NO: 81 is the determined cDNA sequence for LST-S1-A-10D
SEQ ID NO: 82 is the determined cDNA sequence for LST-S1-A-9H
SEQ ID NO: 83 is the determined cDNA sequence for LST-S1-A-11D
SEQ ID NO: 84 is the determined cDNA sequence for LST-S1-A-12D
SEQ ID NO: 85 is the determined cDNA sequence for LST-S1-A-11E
30 SEQ ID NO: 86 is the determined cDNA sequence for LST-S1-A-12E
SEQ ID NO: 87 is the determined cDNA sequence for L513S (T3).

SEQ ID NO: 88 is the determined cDNA sequence for L513S contig 1.

SEQ ID NO: 89 is a first determined cDNA sequence for L514S.

SEQ ID NO: 90 is a second determined cDNA sequence for L514S.

SEQ ID NO: 91 is a first determined cDNA sequence for L516S.

5 SEQ ID NO: 92 is a second determined cDNA sequence for L516S.

SEQ ID NO: 93 is the determined cDNA sequence for L517S.

SEQ ID NO: 94 is the extended cDNA sequence for LST-S1-169 (also known as L519S).

SEQ ID NO: 95 is a first determined cDNA sequence for L520S.

10 SEQ ID NO: 96 is a second determined cDNA sequence for L520S.

SEQ ID NO: 97 is a first determined cDNA sequence for L521S.

SEQ ID NO: 98 is a second determined cDNA sequence for L521S.

SEQ ID NO: 99 is the determined cDNA sequence for L522S.

SEQ ID NO: 100 is the determined cDNA sequence for L523S.

15 SEQ ID NO: 101 is the determined cDNA sequence for L524S.

SEQ ID NO: 102 is the determined cDNA sequence for L525S.

SEQ ID NO: 103 is the determined cDNA sequence for L526S.

SEQ ID NO: 104 is the determined cDNA sequence for L527S.

SEQ ID NO: 105 is the determined cDNA sequence for L528S.

20 SEQ ID NO: 106 is the determined cDNA sequence for L529S.

SEQ ID NO: 107 is a first determined cDNA sequence for L530S.

SEQ ID NO: 108 is a second determined cDNA sequence for L530S.

SEQ ID NO: 109 is the determined full-length cDNA sequence for L531S short form

SEQ ID NO: 110 is the predicted amino acid sequence encoded by SEQ ID NO: 109.

25 SEQ ID NO: 111 is the determined full-length cDNA sequence for L531S long form

SEQ ID NO: 112 is the predicted amino acid sequence encoded by SEQ ID NO: 111.

SEQ ID NO: 113 is the determined full-length cDNA sequence for L520S.

SEQ ID NO: 114 is the predicted amino acid sequence encoded by SEQ ID NO: 113.

SEQ ID NO: 115 is the determined cDNA sequence for contig 1.

30 SEQ ID NO: 116 is the determined cDNA sequence for contig 3.

SEQ ID NO: 117 is the determined cDNA sequence for contig 4.

- SEQ ID NO: 118 is the determined cDNA sequence for contig 5.
SEQ ID NO: 119 is the determined cDNA sequence for contig 7.
SEQ ID NO: 120 is the determined cDNA sequence for contig 8.
SEQ ID NO: 121 is the determined cDNA sequence for contig 9.
5 SEQ ID NO: 122 is the determined cDNA sequence for contig 10.
SEQ ID NO: 123 is the determined cDNA sequence for contig 12.
SEQ ID NO: 124 is the determined cDNA sequence for contig 11.
SEQ ID NO: 125 is the determined cDNA sequence for contig 13.
SEQ ID NO: 126 is the determined cDNA sequence for contig 15.
10 SEQ ID NO: 127 is the determined cDNA sequence for contig 16.
SEQ ID NO: 128 is the determined cDNA sequence for contig 17.
SEQ ID NO: 129 is the determined cDNA sequence for contig 19.
SEQ ID NO: 130 is the determined cDNA sequence for contig 20.
SEQ ID NO: 131 is the determined cDNA sequence for contig 22.
15 SEQ ID NO: 132 is the determined cDNA sequence for contig 24.
SEQ ID NO: 133 is the determined cDNA sequence for contig 29.
SEQ ID NO: 134 is the determined cDNA sequence for contig 31.
SEQ ID NO: 135 is the determined cDNA sequence for contig 33.
SEQ ID NO: 136 is the determined cDNA sequence for contig 38.
20 SEQ ID NO: 137 is the determined cDNA sequence for contig 39.
SEQ ID NO: 138 is the determined cDNA sequence for contig 41.
SEQ ID NO: 139 is the determined cDNA sequence for contig 43.
SEQ ID NO: 140 is the determined cDNA sequence for contig 44.
SEQ ID NO: 141 is the determined cDNA sequence for contig 45.
25 SEQ ID NO: 142 is the determined cDNA sequence for contig 47.
SEQ ID NO: 143 is the determined cDNA sequence for contig 48.
SEQ ID NO: 144 is the determined cDNA sequence for contig 49.
SEQ ID NO: 145 is the determined cDNA sequence for contig 50.
SEQ ID NO: 146 is the determined cDNA sequence for contig 53.
30 SEQ ID NO: 147 is the determined cDNA sequence for contig 54.
SEQ ID NO: 148 is the determined cDNA sequence for contig 56.

- SEQ ID NO: 149 is the determined cDNA sequence for contig 57.
- SEQ ID NO: 150 is the determined cDNA sequence for contig 58.
- SEQ ID NO: 151 is the full-length cDNA sequence for L530S.
- SEQ ID NO: 152 is the amino acid sequence encoded by SEQ ID NO: 151
- 5 SEQ ID NO: 153 is the full-length cDNA sequence of a first variant of L514S
- SEQ ID NO: 154 is the full-length cDNA sequence of a second variant of L514S
- SEQ ID NO: 155 is the amino acid sequence encoded by SEQ ID NO: 153.
- SEQ ID NO: 156 is the amino acid sequence encoded by SEQ ID NO: 154.
- SEQ ID NO: 157 is the determined cDNA sequence for contig 59.
- 10 SEQ ID NO: 158 is the full-length cDNA sequence for L763P (also referred to as contig 22).
- SEQ ID NO: 159 is the amino acid sequence encoded by SEQ ID NO: 158.
- SEQ ID NO: 160 is the full-length cDNA sequence for L762P (also referred to as contig 17).
- 15 SEQ ID NO: 161 is the amino acid sequence encoded by SEQ ID NO: 160.
- SEQ ID NO: 162 is the determined cDNA sequence for L515S.
- SEQ ID NO: 163 is the full-length cDNA sequence of a first variant of L524S.
- SEQ ID NO: 164 is the full-length cDNA sequence of a second variant of L524S.
- SEQ ID NO: 165 is the amino acid sequence encoded by SEQ ID NO: 163.
- 20 SEQ ID NO: 166 is the amino acid sequence encoded by SEQ ID NO: 164.
- SEQ ID NO: 167 is the full-length cDNA sequence of a first variant of L762P.
- SEQ ID NO: 168 is the full-length cDNA sequence of a second variant of L762P.
- SEQ ID NO: 169 is the amino acid sequence encoded by SEQ ID NO: 167.
- SEQ ID NO: 170 is the amino acid sequence encoded by SEQ ID NO: 168.
- 25 SEQ ID NO: 171 is the full-length cDNA sequence for L773P (also referred to as contig 56).
- SEQ ID NO: 172 is the amino acid sequence encoded by SEQ ID NO: 171.
- SEQ ID NO: 173 is an extended cDNA sequence for L519S.
- SEQ ID NO: 174 is the predicted amino acid sequence encoded by SEQ ID NO: 174.
- 30 SEQ ID NO: 175 is the full-length cDNA sequence for L523S.
- SEQ ID NO: 176 is the predicted amino acid sequence encoded by SEQ ID NO: 175.

- SEQ ID NO: 177 is the determined cDNA sequence for LST-sub5-7A.
SEQ ID NO: 178 is the determined cDNA sequence for LST-sub5-8G.
SEQ ID NO: 179 is the determined cDNA sequence for LST-sub5-8H.
SEQ ID NO: 180 is the determined cDNA sequence for LST-sub5-10B.
5 SEQ ID NO: 181 is the determined cDNA sequence for LST-sub5-10H.
SEQ ID NO: 182 is the determined cDNA sequence for LST-sub5-12B.
SEQ ID NO: 183 is the determined cDNA sequence for LST-sub5-11C.
SEQ ID NO: 184 is the determined cDNA sequence for LST-sub6-1c.
SEQ ID NO: 185 is the determined cDNA sequence for LST-sub6-2f.
10 SEQ ID NO: 186 is the determined cDNA sequence for LST-sub6-2G.
SEQ ID NO: 187 is the determined cDNA sequence for LST-sub6-4d.
SEQ ID NO: 188 is the determined cDNA sequence for LST-sub6-4e.
SEQ ID NO: 189 is the determined cDNA sequence for LST-sub6-4f.
SEQ ID NO: 190 is the determined cDNA sequence for LST-sub6-3h.
15 SEQ ID NO: 191 is the determined cDNA sequence for LST-sub6-5d.
SEQ ID NO: 192 is the determined cDNA sequence for LST-sub6-5h.
SEQ ID NO: 193 is the determined cDNA sequence for LST-sub6-6h.
SEQ ID NO: 194 is the determined cDNA sequence for LST-sub6-7a.
SEQ ID NO: 195 is the determined cDNA sequence for LST-sub6-8a.
20 SEQ ID NO: 196 is the determined cDNA sequence for LST-sub6-7d.
SEQ ID NO: 197 is the determined cDNA sequence for LST-sub6-7e.
SEQ ID NO: 198 is the determined cDNA sequence for LST-sub6-8e.
SEQ ID NO: 199 is the determined cDNA sequence for LST-sub6-7g.
SEQ ID NO: 200 is the determined cDNA sequence for LST-sub6-9f.
25 SEQ ID NO: 201 is the determined cDNA sequence for LST-sub6-9h.
SEQ ID NO: 202 is the determined cDNA sequence for LST-sub6-11b.
SEQ ID NO: 203 is the determined cDNA sequence for LST-sub6-11c.
SEQ ID NO: 204 is the determined cDNA sequence for LST-sub6-12c.
SEQ ID NO: 205 is the determined cDNA sequence for LST-sub6-12e.
30 SEQ ID NO: 206 is the determined cDNA sequence for LST-sub6-12f.
SEQ ID NO: 207 is the determined cDNA sequence for LST-sub6-11g.

- SEQ ID NO: 208 is the determined cDNA sequence for LST-sub6-12g.
SEQ ID NO: 209 is the determined cDNA sequence for LST-sub6-12h.
SEQ ID NO: 210 is the determined cDNA sequence for LST-sub6-II-1a.
SEQ ID NO: 211 is the determined cDNA sequence for LST-sub6-II-2b.
5 SEQ ID NO: 212 is the determined cDNA sequence for LST-sub6-II-2g.
SEQ ID NO: 213 is the determined cDNA sequence for LST-sub6-II-1h.
SEQ ID NO: 214 is the determined cDNA sequence for LST-sub6-II-4a.
SEQ ID NO: 215 is the determined cDNA sequence for LST-sub6-II-4b.
SEQ ID NO: 216 is the determined cDNA sequence for LST-sub6-II-3e.
10 SEQ ID NO: 217 is the determined cDNA sequence for LST-sub6-II-4f.
SEQ ID NO: 218 is the determined cDNA sequence for LST-sub6-II-4g.
SEQ ID NO: 219 is the determined cDNA sequence for LST-sub6-II-4h.
SEQ ID NO: 220 is the determined cDNA sequence for LST-sub6-II-5c.
SEQ ID NO: 221 is the determined cDNA sequence for LST-sub6-II-5e.
15 SEQ ID NO: 222 is the determined cDNA sequence for LST-sub6-II-6f.
SEQ ID NO: 223 is the determined cDNA sequence for LST-sub6-II-5g.
SEQ ID NO: 224 is the determined cDNA sequence for LST-sub6-II-6g.
SEQ ID NO: 225 is the amino acid sequence for L528S.
SEQ ID NO: 226-251 are synthetic peptides derived from L762P.
20 SEQ ID NO: 252 is the expressed amino acid sequence of L514S.
SEQ ID NO: 253 is the DNA sequence corresponding to SEQ ID NO: 252.
SEQ ID NO: 254 is the DNA sequence of a L762P expression construct.
SEQ ID NO: 255 is the determined cDNA sequence for clone 23785.
SEQ ID NO: 256 is the determined cDNA sequence for clone 23786.
25 SEQ ID NO: 257 is the determined cDNA sequence for clone 23788.
SEQ ID NO: 258 is the determined cDNA sequence for clone 23790.
SEQ ID NO: 259 is the determined cDNA sequence for clone 23793.
SEQ ID NO: 260 is the determined cDNA sequence for clone 23794.
SEQ ID NO: 261 is the determined cDNA sequence for clone 23795.
30 SEQ ID NO: 262 is the determined cDNA sequence for clone 23796.
SEQ ID NO: 263 is the determined cDNA sequence for clone 23797.

- SEQ ID NO: 264 is the determined cDNA sequence for clone 23798.
SEQ ID NO: 265 is the determined cDNA sequence for clone 23799.
SEQ ID NO: 266 is the determined cDNA sequence for clone 23800.
SEQ ID NO: 267 is the determined cDNA sequence for clone 23802.
5 SEQ ID NO: 268 is the determined cDNA sequence for clone 23803.
SEQ ID NO: 269 is the determined cDNA sequence for clone 23804.
SEQ ID NO: 270 is the determined cDNA sequence for clone 23805.
SEQ ID NO: 271 is the determined cDNA sequence for clone 23806.
SEQ ID NO: 272 is the determined cDNA sequence for clone 23807.
10 SEQ ID NO: 273 is the determined cDNA sequence for clone 23808.
SEQ ID NO: 274 is the determined cDNA sequence for clone 23809.
SEQ ID NO: 275 is the determined cDNA sequence for clone 23810.
SEQ ID NO: 276 is the determined cDNA sequence for clone 23811.
SEQ ID NO: 277 is the determined cDNA sequence for clone 23812.
15 SEQ ID NO: 278 is the determined cDNA sequence for clone 23813.
SEQ ID NO: 279 is the determined cDNA sequence for clone 23815.
SEQ ID NO: 280 is the determined cDNA sequence for clone 25298.
SEQ ID NO: 281 is the determined cDNA sequence for clone 25299.
SEQ ID NO: 282 is the determined cDNA sequence for clone 25300.
20 SEQ ID NO: 283 is the determined cDNA sequence for clone 25301
SEQ ID NO: 284 is the determined cDNA sequence for clone 25304
SEQ ID NO: 285 is the determined cDNA sequence for clone 25309.
SEQ ID NO: 286 is the determined cDNA sequence for clone 25312.
SEQ ID NO: 287 is the determined cDNA sequence for clone 25317.
25 SEQ ID NO: 288 is the determined cDNA sequence for clone 25321.
SEQ ID NO: 289 is the determined cDNA sequence for clone 25323.
SEQ ID NO: 290 is the determined cDNA sequence for clone 25327.
SEQ ID NO: 291 is the determined cDNA sequence for clone 25328.
SEQ ID NO: 292 is the determined cDNA sequence for clone 25332.
30 SEQ ID NO: 293 is the determined cDNA sequence for clone 25333.
SEQ ID NO: 294 is the determined cDNA sequence for clone 25336.

- SEQ ID NO: 295 is the determined cDNA sequence for clone 25340.
SEQ ID NO: 296 is the determined cDNA sequence for clone 25342.
SEQ ID NO: 297 is the determined cDNA sequence for clone 25356.
SEQ ID NO: 298 is the determined cDNA sequence for clone 25357.
5 SEQ ID NO: 299 is the determined cDNA sequence for clone 25361.
SEQ ID NO: 300 is the determined cDNA sequence for clone 25363.
SEQ ID NO: 301 is the determined cDNA sequence for clone 25397.
SEQ ID NO: 302 is the determined cDNA sequence for clone 25402.
SEQ ID NO: 303 is the determined cDNA sequence for clone 25403.
10 SEQ ID NO: 304 is the determined cDNA sequence for clone 25405.
SEQ ID NO: 305 is the determined cDNA sequence for clone 25407.
SEQ ID NO: 306 is the determined cDNA sequence for clone 25409.
SEQ ID NO: 307 is the determined cDNA sequence for clone 25396.
SEQ ID NO: 308 is the determined cDNA sequence for clone 25414.
15 SEQ ID NO: 309 is the determined cDNA sequence for clone 25410.
SEQ ID NO: 310 is the determined cDNA sequence for clone 25406.
SEQ ID NO: 311 is the determined cDNA sequence for clone 25306.
SEQ ID NO: 312 is the determined cDNA sequence for clone 25362.
SEQ ID NO: 313 is the determined cDNA sequence for clone 25360.
20 SEQ ID NO: 314 is the determined cDNA sequence for clone 25398.
SEQ ID NO: 315 is the determined cDNA sequence for clone 25355.
SEQ ID NO: 316 is the determined cDNA sequence for clone 25351.
SEQ ID NO: 317 is the determined cDNA sequence for clone 25331.
SEQ ID NO: 318 is the determined cDNA sequence for clone 25338.
25 SEQ ID NO: 319 is the determined cDNA sequence for clone 25335.
SEQ ID NO: 320 is the determined cDNA sequence for clone 25329.
SEQ ID NO: 321 is the determined cDNA sequence for clone 25324.
SEQ ID NO: 322 is the determined cDNA sequence for clone 25322.
SEQ ID NO: 323 is the determined cDNA sequence for clone 25319.
30 SEQ ID NO: 324 is the determined cDNA sequence for clone 25316.
SEQ ID NO: 325 is the determined cDNA sequence for clone 25311.

- SEQ ID NO: 326 is the determined cDNA sequence for clone 25310.
SEQ ID NO: 327 is the determined cDNA sequence for clone 25302.
SEQ ID NO: 328 is the determined cDNA sequence for clone 25315.
SEQ ID NO: 329 is the determined cDNA sequence for clone 25308.
5 SEQ ID NO: 330 is the determined cDNA sequence for clone 25303.
SEQ ID NO: 331-337 are the cDNA sequences of isoforms of the p53 tumor suppressor homologue, p63 (also referred to as L530S).
SEQ ID NO: 338-344 are the amino acid sequences encoded by SEQ ID NO: 331-337, respectively.
10 SEQ ID NO: 345 is a second cDNA sequence for the antigen L763P.
SEQ ID NO: 346 is the amino acid sequence encoded by the sequence of SEQ ID NO: 345.
SEQ ID NO: 347 is a determined full-length cDNA sequence for L523S.
SEQ ID NO: 348 is the predicted amino acid sequence encoded by SEQ ID NO: 347.
15 SEQ ID NO: 349 is the cDNA sequence encoding the N-terminal portion of L773P.
SEQ ID NO: 350 is the amino acid sequence of the N-terminal portion of L773P.

DETAILED DESCRIPTION OF THE INVENTION

- As noted above, the present invention is generally directed to
20 compositions and methods for the therapy and diagnosis of cancer, such as lung cancer. The compositions described herein may include lung tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic
25 portion) of a lung tumor protein or a variant thereof. A "lung tumor protein" is a protein that is expressed in lung tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain lung tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western
30 blot) with antisera of a patient afflicted with lung cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of

such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery human lung tumor proteins. Sequences of polynucleotides encoding specific tumor proteins are provided in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349.

LUNG TUMOR PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a lung tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a lung tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a lung tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a lung tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the

encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native lung tumor protein or a portion thereof. The term “variants” also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be “identical” if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A “comparison window” as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) *Unified Approach to Alignment and Phylogenies* pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Preferably, the “percentage of sequence identity” is determined by comparing two optimally aligned sequences over a window of comparison of at least 20

positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native lung tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (i.e., expression that

is at least two fold greater in a lung tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and
5 Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as lung tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

10 An amplified portion may be used to isolate a full length gene from a suitable library (e.g., a lung tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be
15 preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with ³²P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured
20 bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using
25 a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be
30 generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs

may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

Certain nucleic acid sequences of cDNA molecules encoding portions of lung tumor proteins are provided in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (*see* Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a lung tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (*e.g.*, by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a lung tumor polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (*see* Gee et al., *In Huber and Carr, Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (*e.g.*, promoter, enhancer or transcription

initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled
5 with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*.
10 Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

15 Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation
20 vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to
25 permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not
30 limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus).). The polynucleotides may also be administered as naked

plasmid vectors. Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

15 LUNG TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a lung tumor protein or a variant thereof, as described herein. As noted above, a "lung tumor protein" is a protein that is expressed by lung tumor cells. Proteins that are lung tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with lung cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a lung tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may

contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-
5 247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins).
10 Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native lung tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is
15 similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the
20 sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

As noted above, a composition may comprise a variant of a native lung tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native lung tumor protein in one or more substitutions, deletions, additions
25 and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above
30 polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include

those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

5 Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

 Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydrophathic nature of the polypeptide.

 As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the

polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above
5 may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells. Preferably, the host
10 cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or
15 more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example,
20 such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems
25 Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known
30 tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans,

or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second

polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see*, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible

for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see
5 *Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides
10 as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is
15 considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and
20 antigen-binding fragments thereof, that specifically bind to a lung tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a lung tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a lung tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association
25 between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding
30 constant for complex formation exceeds about 10^3 L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as lung cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a lung tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, sputum urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically.

Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest
5 may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as
10 described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid
15 cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

20 Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by
25 conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be
30 prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane,

Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or
5 more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria
10 toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a
15 substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an
20 antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents,
25 which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups,
30 sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a lung tumor protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a lung tumor polypeptide, polynucleotide encoding a lung tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a lung tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a lung tumor polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell

proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a lung tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in
5 at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN-γ) is indicative of T cell activation (*see* Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been
10 activated in response to a lung tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Lung tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

15 For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a lung tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a lung tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such
20 a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a lung tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a lung tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

25

PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise
30 one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant

may be any substance that enhances or potentiates an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl.*

Acad. Sci. USA 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 5 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier 10 will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. 15 For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (*e.g.*, polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres 20 are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (*e.g.*, neutral buffered saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (*e.g.*, aluminum hydroxide) 25 and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a 30 substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A,

Bordetella pertussis or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA);
5 aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

10 Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the
15 induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using
20 standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt.
25 MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT) (see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555 and WO 99/33488. Immunostimulatory DNA sequences
30 are also described, for example, by Sato et al., *Science* 273:352, 1996. Another preferred adjuvant is a saponin, preferably QS21 (Aquila Biopharmaceuticals Inc.,

Framingham, MA), which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Other preferred adjuvants include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (*e.g.*, SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Ribi ImmunoChem Research Inc., Hamilton, MT), RC-529 (Ribi ImmunoChem Research Inc., Hamilton, MT) and Aminoalkyl glucosaminide 4-phosphates (AGPs).

Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient. The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides, for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology (*see, e.g.* Coombes et al., *Vaccine* 14:1429-1438, 1996) and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane.

Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. Such carriers include microparticles of poly(lactide-co-glycolide), as well as polyacrylate, latex, starch, cellulose and dextran. Other delayed-release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and, optionally,

an external layer comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA-haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood,

bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes
5 harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

10 Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which
15 correlates with the high expression of Fc γ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

20 APCs may generally be transfected with a polynucleotide encoding a lung tumor protein (or portion or other variant thereof) such that the lung tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein.
25 Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell*
30 *Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the lung tumor polypeptide, DNA

(naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

Vaccines and pharmaceutical compositions may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are preferably hermetically sealed to preserve sterility of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a vaccine or pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier, immediately prior to use.

15 CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as lung cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive

long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 μ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free

survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a lung tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more lung tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as lung cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a lung tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent

that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length lung tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 μ g, and preferably about 100 ng to about 1 μ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the

binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook, 1991, at
5 A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody.
10 Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

15 More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to
20 bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.,* incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with lung cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of
25 that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

30 Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second

antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as lung cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered

positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

5 In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution
10 containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent.
15 Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the
20 biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about
25 500 ng. Such tests can typically be performed with a very small amount of biological sample.

 Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to
30 those of ordinary skill in the art that the above protocols may be readily modified to use lung tumor polypeptides to detect antibodies that bind to such polypeptides in a

biological sample. The detection of such lung tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a lung tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a lung tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide, (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of lung tumor polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a lung tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a lung tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (i.e., hybridizes to) a polynucleotide encoding the lung tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a lung tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%,

preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a lung tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed
5 herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a
10 sequence recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

15 One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification
20 may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered
25 positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be
30 performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the

level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor.

5 One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple lung tumor protein
10 markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins
15 provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components
20 necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a lung tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements,
25 such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a lung tumor protein in a biological sample. Such kits generally comprise at
30 least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a lung tumor protein. Such an oligonucleotide may be used,

for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a lung tumor protein.

The following Examples are offered by way of illustration and not by
5 way of limitation.

EXAMPLE 1
ISOLATION AND CHARACTERIZATION OF cDNA SEQUENCES
ENCODING LUNG TUMOR POLYPEPTIDES

5

This example illustrates the isolation of cDNA molecules encoding lung tumor-specific polypeptides from lung tumor cDNA libraries.

A. ISOLATION OF cDNA SEQUENCES FROM A LUNG SQUAMOUS CELL
10 CARCINOMA LIBRARY

A human lung squamous cell carcinoma cDNA expression library was constructed from poly A⁺ RNA from a pool of two patient tissues using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD) following the manufacturer's protocol. Specifically, lung carcinoma
15 tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A⁺ RNA was then purified using an oligo dT cellulose column as described in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989. First-strand cDNA was
20 synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with BstXI/EcoRI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with cDNA size fractionation columns (BRL Life Technologies), the cDNA was ligated into the BstXI/NotI site of pcDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life
25 Technologies) by electroporation.

Using the same procedure, a normal human lung cDNA expression library was prepared from a pool of four tissue specimens. The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The lung
30 squamous cell carcinoma library contained 2.7×10^6 independent colonies, with 100% of clones having an insert and the average insert size being 2100 base pairs. The normal

lung cDNA library contained 1.4×10^6 independent colonies, with 90% of clones having inserts and the average insert size being 1800 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA

5 cDNA library subtraction was performed using the above lung squamous cell carcinoma and normal lung cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a lung squamous cell carcinoma-specific subtracted cDNA library was generated as follows. Normal tissue cDNA library (80 μ g) was digested with BamHI and XhoI, followed by a filling-in
10 reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 133 μ l of H₂O, heat-denatured and mixed with 133 μ l (133 μ g) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (67 μ l) was added
15 and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 μ l H₂O to form the driver DNA.

To form the tracer DNA, 10 μ g lung squamous cell carcinoma cDNA library was digested with NotI and SpeI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech, Palo Alto, CA). Typically, 5 μ g of
20 cDNA was recovered after the sizing column. Following ethanol precipitation, the tracer DNA was dissolved in 5 μ l H₂O. Tracer DNA was mixed with 15 μ l driver DNA and 20 μ l of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and
25 incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 μ l H₂O, mixed with 8 μ l driver DNA and 20 μ l of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After
30 removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into NotI/SpeI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA) and

transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a lung squamous cell carcinoma specific subtracted cDNA library (herein after referred to as "lung subtraction I").

5 A second lung squamous cell carcinoma specific subtracted cDNA library (referred to as "lung subtraction II") was generated in a similar way to the lung subtraction library I, except that eight frequently recovered genes from lung subtraction I were included in the driver DNA, and 24,000 independent clones were recovered.

To analyze the subtracted cDNA libraries, plasmid DNA was prepared from 320 independent clones, randomly picked from the subtracted lung squamous cell carcinoma specific libraries. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A and/or Model 377 (Foster City, CA). The cDNA sequences for sixty isolated clones are provided in SEQ ID NO: 1-60. These sequences were compared to known sequences in the gene bank using the EMBL and GenBank
10 databases (release 96). No significant homologies were found to the sequences provided in SEQ ID NO: 2, 3, 19, 38 and 46. The sequences of SEQ ID NO: 1, 6-8, 10-13, 15, 17, 18, 20-27, 29, 30, 32, 34-37, 39-45, 47-49, 51, 52, 54, 55 and 57-59 were found to show some homology to previously identified expressed sequence tags (ESTs). The sequences of SEQ ID NO: 9, 28, 31 and 33 were found to show some homology to
15 previously identified non-human gene sequences and the sequences of SEQ ID NO: 4, 5, 14, 50, 53, 56 and 60 were found to show some homology to gene sequences previously identified in humans.

The subtraction procedure described above was repeated using the above lung squamous cell carcinoma cDNA library as the tracer DNA, and the above normal lung tissue cDNA library and a cDNA library from normal liver and heart (constructed from a pool of one sample of each tissue as described above), plus twenty other cDNA clones that were frequently recovered in lung subtractions I and II, as the driver DNA (lung subtraction III). The normal liver and heart cDNA library contained 1.76×10^6 independent colonies, with 100% of clones having inserts and the average insert size
25 being 1600 base pairs. Ten additional clones were isolated (SEQ ID NO: 61-70). Comparison of these cDNA sequences with those in the gene bank as described above,

30

revealed no significant homologies to the sequences provided in SEQ ID NO: 62 and 67. The sequences of SEQ ID NO: 61, 63-66, 68 and 69 were found to show some homology to previously isolated ESTs and the sequence provided in SEQ ID NO: 70 was found to show some homology to a previously identified rat gene.

5 In further studies, the subtraction procedure described above was repeated using the above lung squamous cell carcinoma cDNA library as the tracer DNA, and a cDNA library from a pool of normal lung, kidney, colon, pancreas, brain, resting PBMC, heart, skin and esophagus as the driver DNA, with esophagus cDNAs making up one third of the driver material. Since esophagus is enriched in normal
10 epithelial cells, including differentiated squamous cells, this procedure is likely to enrich genes that are tumor specific rather than tissues specific. The cDNA sequences of 48 clones determined in this subtraction are provided in SEQ ID NO: 177-224. The sequences of SEQ ID NO: 177, 178, 180, 181, 183, 187, 192, 195-197, 208, 211, 212, 215, 216, 218 and 219 showed some homology to previously identified genes. The
15 sequences of SEQ ID NO: 179, 182, 184-186, 188-191, 193, 194, 198-207, 209 210, 213, 214, 217, 220 and 224 showed some homology to previously determined ESTs. The sequence of SEQ ID NO: 221-223 showed no homology to any previously determined sequence.

20 B. ISOLATION OF cDNA SEQUENCES FROM A LUNG ADENOCARCINOMA LIBRARY

A human lung adenocarcinoma cDNA expression library was constructed as described above. The library contained 3.2×10^6 independent colonies, with 100% of clones having an insert and the average insert size being 1500 base pairs.
25 Library subtraction was performed as described above using the normal lung and normal liver and heart cDNA expression libraries described above as the driver DNA. Twenty-six hundred independent clones were recovered.

Initial cDNA sequence analysis from 100 independent clones revealed many ribosomal protein genes. The cDNA sequences for fifteen clones isolated in this
30 subtraction are provided in SEQ ID NO: 71-86. Comparison of these sequences with those in the gene bank as described above revealed no significant homologies to the

sequence provided in SEQ ID NO: 84. The sequences of SEQ ID NO: 71, 73, 74, 77, 78 and 80-82 were found to show some homology to previously isolated ESTs, and the sequences of SEQ ID NO: 72, 75, 76, 79, 83 and 85 were found to show some homology to previously identified human genes.

5 In further studies, a cDNA library (referred to as mets3616A) was constructed from a metastatic lung adenocarcinoma. The determined cDNA sequences of 25 clones sequenced at random from this library are provided in SEQ ID NO: 255-279. The mets3616A cDNA library was subtracted against a cDNA library prepared from a pool of normal lung, liver, pancreas, skin, kidney, brain and resting PBMC. To
10 increase the specificity of the subtraction, the driver was spiked with genes that were determined to be most abundant in the mets3616A cDNA library, such as EF1-alpha, integrin-beta and anticoagulant protein PP4, as well as with cDNAs that were previously found to be differentially expressed in subtracted lung adenocarcinoma cDNA libraries. The determined cDNA sequences of 51 clones isolated from the
15 subtracted library (referred to as mets3616A-S1) are provided in SEQ ID NO: 280-330.

Comparison of the sequences of SEQ ID NO: 255-330 with those in the public databases revealed no significant homologies to the sequences of SEQ ID NO: 255-258, 260, 262-264, 270, 272, 275, 276, 279, 281, 287, 291, 296, 300 and 310. The sequences of SEQ ID NO: 259, 261, 265-269, 271, 273, 274, 277, 278, 282-285, 288-
20 290, 292, 294, 297-299, 301, 303-309, 313, 314, 316, 320-324 and 326-330 showed some homology to previously identified gene sequences, while the sequences of SEQ ID NO: 280, 286, 293, 302, 310, 312, 315, 317-319 and 325 showed some homology to previously isolated expressed sequence tags (ESTs).

25

EXAMPLE 2

DETERMINATION OF TISSUE SPECIFICITY OF LUNG TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for seven
30 representative lung tumor polypeptides described in Example 1 were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 2 µg of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β-actin was used as an internal control for each of the tissues examined. 1 µl of 1:30 dilution of cDNA was employed to enable the linear range amplification of the β-actin template and was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β-actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in five different types of tumor tissue (lung squamous cell carcinoma from 3 patients, lung adenocarcinoma, colon tumor from 2 patients, breast tumor and prostate tumor), and thirteen different normal tissues (lung from 4 donors, prostate, brain, kidney, liver, ovary, skeletal muscle, skin, small intestine, stomach, myocardium, retina and testes). Using a 10-fold amount of cDNA, the antigen LST-S1-90 (SEQ ID NO: 3) was found to be expressed at high levels in lung squamous cell carcinoma and in breast tumor, and at low to undetectable levels in the other tissues examined.

The antigen LST-S2-68 (SEQ ID NO: 15) appears to be specific to lung and breast tumor, however, expression was also detected in normal kidney. Antigens LST-S1-169 (SEQ ID NO: 6) and LST-S1-133 (SEQ ID NO: 5) appear to be very abundant in lung tissues (both normal and tumor), with the expression of these two genes being decreased in most of the normal tissues tested. Both LST-S1-169 and LST-S1-133 were also expressed in breast and colon tumors. Antigens LST-S1-6 (SEQ ID NO: 7) and LST-S2-I2-5F (SEQ ID NO: 47) did not show tumor or tissue specific expression, with the expression of LST-S1-28 being rare and only detectable in a few tissues. The antigen LST-S3-7 (SEQ ID NO: 63) showed lung and breast tumor specific expression, with its message only being detected in normal testes when the PCR was performed for 30 cycles. Lower level expression was detected in some

normal tissues when the cycle number was increased to 35. Antigen LST-S3-13 (SEQ ID NO: 66) was found to be expressed in 3 out of 4 lung tumors, one breast tumor and both colon tumor samples. Its expression in normal tissues was lower compared to tumors, and was only detected in 1 out of 4 normal lung tissues and in normal tissues from kidney, ovary and retina. Expression of antigens LST-S3-4 (SEQ ID NO: 62) and LST-S3-14 (SEQ ID NO: 67) was rare and did not show any tissue or tumor specificity. Consistent with Northern blot analyses, the RT-PCT results on antigen LAT-S1-A-10A (SEQ ID NO: 78) suggested that its expression is high in lung, colon, stomach and small intestine tissues, including lung and colon tumors, whereas its expression was low or undetectable in other tissues.

A total of 2002 cDNA fragments isolated in lung subtractions I, II and III, described above, were colony PCR amplified and their mRNA expression levels in lung tumor, normal lung, and various other normal and tumor tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Seventeen non-redundant cDNA clones showed over-expression in lung squamous tumors, with expression in normal tissues tested (lung, skin, lymph node, colon, liver, pancreas, breast, heart, bone marrow, large intestine, kidney, stomach, brain, small intestine, bladder and salivary gland) being either undetectable, or 10-fold less compared to lung squamous tumors. The determined partial cDNA sequences for the clone L513S are provided in SEQ ID NO: 87 and 88; those for L514S are provided in SEQ ID NO: 89 and 90; those for L516S in SEQ ID NO: 91 and 92; that for L517S in SEQ ID NO: 93; that for L519S in SEQ ID NO: 94; those for L520S in SEQ ID NO: 95 and 96; those for L521S in SEQ ID NO: 97 and 98; that for L522S in SEQ ID NO: 99; that for L523S in SEQ ID NO: 100; that for L524S in SEQ ID NO: 101; that for L525S in SEQ ID NO: 102; that for L526S in SEQ ID NO: 103; that for L527S in SEQ ID NO: 104; that for L528S in SEQ ID NO: 105; that for L529S in SEQ ID NO: 106;

and those for L530S in SEQ ID NO: 107 and 108. Additionally, the full-length cDNA sequence for L530S is provided in SEQ ID NO: 151, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 152. L530S shows homology to a splice variant of a p53 tumor suppressor homologue, p63. The cDNA sequences of 7
5 known isoforms of p63 are provided in SEQ ID NO: 331-337, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 338-344, respectively.

Due to polymorphisms, the clone L531S appears to have two forms. A first determined full-length cDNA sequence for L531S is provided in SEQ ID NO: 109, with the corresponding predicted amino acid sequence being provided in SEQ ID NO:
10 110. A second determined full-length cDNA sequence for L531S is provided in SEQ ID NO: 111, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 112. The sequence of SEQ ID NO: 111 is identical to that of SEQ ID NO: 109, except that it contains a 27 bp insertion. Similarly, L514S also has two alternatively spliced forms; the first variant cDNA is listed as SEQ ID NO: 153, with
15 the corresponding amino acid sequence being provided in SEQ ID NO: 155. The second variant form of L514S full-length cDNA is provided in SEQ ID NO: 154, with its corresponding amino acid sequence being provided in SEQ ID NO: 156.

Full length cloning for L524S (SEQ ID NO: 101) yielded two variants (SEQ ID NO: 163 and 164) with the corresponding predicted amino acid sequences of
20 SEQ ID NO: 165 and 166, respectively. Both variants have been shown to encode parathyroid hormone-related peptide.

Attempts to isolate the full-length cDNA for L519S, resulted in the isolation of the extended cDNA sequence provided in SEQ ID NO: 173, which contains a potential open reading frame. The predicted amino acid sequence encoded by the
25 sequence of SEQ ID NO: 173 is provided in SEQ ID NO: 174. Additionally, the full-length cDNA sequence for the clone of SEQ ID NO: 100 (known as L523S), a known gene, is provided in SEQ ID NO: 175, with the corresponding predicted amino acid sequence provided in SEQ ID NO: 176. In further studies, a full-length cDNA sequence for L523S was isolated from a L523S-positive tumor cDNA library by PCR
30 amplification using gene specific primers designed from the sequence of SEQ ID NO: 175. The determined cDNA sequence is provided in SEQ ID NO: **. The amino acid

sequence encoded by this sequence is provided in SEQ ID NO: **. This protein sequence differs from the previously published protein sequence at two amino acid positions, namely at positions 158 and 410.

Comparison of the sequences of L514S and L531S (SEQ ID NO: 87 and 88, 89 and 90, and 109, respectively) with those in the gene bank, as described above, revealed no significant homologies to known sequences. The sequences of L513S, L516S, L517S, L519S, L520S and L530S (SEQ ID NO: 87 and 88, 91 and 92, 93, 94, 95 and 96, 107 and 108, respectively) were found to show some homology to previously identified ESTs. The sequences of L521S, L522S, L523S, L524S, L525S, L526S, L527S, L528S and L529S (SEQ ID NO: 97 and 98, 99, 99, 101, 102, 103, 104, 105, and 106, respectively) were found to represent known genes. The determined full-length cDNA sequences for L520S is provided in SEQ ID NO: 113, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 114. Subsequent microarray analysis has shown L520S to be overexpressed in breast tumors in addition to lung squamous tumors.

Further analysis has demonstrated that L529S (SEQ ID NO: 106 and 115), L525S (SEQ ID NO: 102 and 120) and L527S (SEQ ID NO: 104) are cytoskeletal components and potentially squamous cell specific proteins. L529S is connexin 26, a gap junction protein. It is highly expressed in lung squamous tumor 9688T, and moderately over-expressed in two others. However, lower level expression of connexin 26 is also detectable in normal skin, colon, liver and stomach. The over-expression of connexin 26 in some breast tumors has been reported and a mutated form of L529S may result in over-expression in lung tumors. L525S is plakophilin 1, a desmosomal protein found in plaque-bearing adhering junctions of the skin. Expression levels for L525S mRNA is highly elevated in three out of four lung squamous tumors tested, and in normal skin. L527S has been identified as keratin 6 isoform, type II 58 Kd keratin, and cytokeratin 13 and shows over-expression in squamous tumors and low expression in normal skin, breast and colon tissues. Notably, keratin and keratin-related genes have been extensively documented as potential markers for lung cancer including CYFRA2.1 (Pastor, A., et al, *Eur. Respir. J.*, 10:603-609, 1997). L513S (SEQ ID NO: 87 and 88)

shows moderate over-expression in several tumor tissues tested, and encodes a protein that was first isolated as a pemphigus vulgaris antigen.

L520S (SEQ ID NO: 95 and 96) and L521S (SEQ ID NO: 97 and 98) are highly expressed in lung squamous tumors, and L520S is up-regulated in normal salivary gland and L521S is over-expressed in normal skin. Both belong to a family of small proline rich proteins and represent markers for fully differentiated squamous cells. L521S has been described as a specific marker for lung squamous tumor (Hu, R., et al, *Lung Cancer*, 20:25-30, 1998). L515S (SEQ ID NO: 162) encodes IGF- β 2 and L516S is an aldose reductase homologue and both are moderately expressed in lung squamous tumors and in normal colon. Notably, L516S (SEQ ID NO: 91 and 92) is up-regulated in metastatic tumors but not primary lung adenocarcinoma, an indication of its potential role in metatasis and a potential prognostic marker. L522S (SEQ ID NO: 99) is moderately over-expressed in lung squamous tumors with minimum expression in normal tissues. L522S has been shown to belong to a class IV alcohol dehydrogenase, ADH7, and its expression profile suggests it is a squamous cell specific antigen. L523S (SEQ ID NO: 100) is moderately over-expressed in lung squamous tumor, human pancreatic cancer cell lines and pancreatic cancer tissues, suggesting this gene may be a shared antigen between pancreatic and lung squamous cell cancer.

L524S (SEQ ID NO: 101) is over-expressed in the majority of squamous tumors tested and is homologous with parathyroid hormone-related peptide (PTHrP), which is best known to cause humoral hypercalcaemia associated with malignant tumors such as leukemia, prostate and breast cancer. It is also believed that PTHrP is most commonly associated with squamous carcinoma of lung and rarely with lung adenocarcinoma (Davidson, L.A., et al, *J. Pathol.*, 178: 398-401, 1996). L528S (SEQ ID NO: 105) is highly over-expressed in two lung squamous tumors with moderate expression in two other squamous tumors, one lung adenocarcinoma and some normal tissues, including skin, lymph nodes, heart, stomach and lung. It encodes the NMB gene that is similar to the precursor of melanocyte specific gene Pmel17, wfhich is reported to be preferentially expressed in low-metastatic potential melanoma cell lines. This suggests that L528S may be a shared antigen in both melanoma and lung squamous cell carcinoma. L526S (SEQ ID NO: 103) is overexpressed in all lung

squamous cell tumor tissues tested and has been shown to share homology with a gene (ATM) in which a mutation causes ataxia telangiectasia, a genetic disorder in humans causing a predisposition to cancer, among other symptoms. ATM encodes a protein that activates p53 mediated cell-cycle checkpoint through direct binding and phosphorylation of the p53 molecule. Approximately 40% of lung cancer is associated with p53 mutations, and it is speculated that over-expression of ATM is a result of compensation for loss of p53 function, but it is unknown whether over-expression is the cause of result of lung squamous cell carcinoma. Additionally, expression of L526S (ATM) is also detected in a metastatic but not lung adenocarcinoma, suggesting a role in metastasis.

Expression of L523S (SEQ ID NO: 175), was also examined by real time RT-PCR as described above. In a first study using a panel of lung squamous tumors, L523S was found to be expressed in 4/7 lung squamous tumors, 2/3 head and neck squamous tumors and 2/2 lung adenocarcinomas, with low level expression being observed in skeletal muscle, soft palate and tonsil. In a second study using a lung adenocarcinoma panel, expression of L523S was observed in 4/9 primary adenocarcinomas, 2/2 lung pleural effusions, 1/1 metastatic lung adenocarcinomas and 2/2 lung squamous tumors, with little expression being observed in normal tissues.

Expression of L523S in lung tumors and various normal tissues was also examined by Northern blot analysis, using standard techniques. In a first study, L523S was found to be expressed in a number of lung adenocarcinomas and squamous cell carcinomas, as well as normal tonsil. No expression was observed in normal lung. In a second study using a normal tissue blot (HB-12) from Clontech, no expression was observed in brain, skeletal muscle, colon, thymus, spleen, kidney, liver, small intestine, lung or PBMC, although there was strong expression in placenta.

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF LUNG TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

Eight hundred and fifty seven clones from a cDNA subtraction library, containing cDNA from a pool of two human lung squamous tumors subtracted against eight normal human tissue cDNAs including lung, PBMC, brain, heart, kidney, liver, pancreas, and skin, (Clontech, Palo Alto, CA) were derived and submitted to a first round of PCR amplification. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector P7- Adv vector (Clontech, Palo Alto, CA) and transformed into DH5 α *E. coli* (Gibco, BRL). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

One hundred and sixty two positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the the EMBL and GenBank databases, as described above, revealed no significant homologies to 13 of these clones, hereinafter referred to as Contigs 13, 16, 17, 19, 22, 24, 29, 47, 49, 56-59. The determined cDNA sequences for these clones are provided in SEQ ID NO: 125, 127-129, 131-133, 142, 144, 148-150, and 157, respectively. Contigs 1, 3-5, 7-10, 12, 11, 15, 20, 31, 33, 38, 39, 41, 43, 44, 45, 48, 50, 53, 54 (SEQ ID NO: 115-124, 126, 130, 134-141, 143, 145-147, respectively) were found to show some degree of homology to previously identified DNA sequences. Contig 57 (SEQ ID NO: 149) was found to represent the clone L519S (SEQ ID NO: 94) disclosed in US. Patent Application No. 09/123,912, filed July 27, 1998. To the best of the inventors' knowledge, none of these sequences have been previously shown to be differentially over-expressed in lung tumors.

mRNA expression levels for representative clones in lung tumor tissues, normal lung tissues (n=4), resting PBMC, salivary gland, heart, stomach, lymph nodes, skeletal muscle, soft palate, small intestine, large intestine, bronchial, bladder, tonsil, kidney, esophagus, bone marrow, colon, adrenal gland, pancreas, and skin, (all derived from human) were determined by RT-PCR as described above. Expression levels using microarray technology, as described above, were examined in one sample of each tissue type unless otherwise indicated.

Contig 3 (SEQ ID NO: 116) was found to be highly expressed in all head and neck squamous cell tumors tested (17/17), and expressed in the majority (8/12) of lung squamous tumors, (high expression in 7/12, moderate in 2/12, and low in 2/12), while showing negative expression for 2/4 normal lung tissues and low expression in the remaining two samples. Contig 3 showed moderate expression in skin and soft palate, and lowered expression levels in resting PBMC, large intestine, salivary gland, tonsil, pancreas, esophagus, and colon. Contig 11 (SEQ ID NO: 124) was found to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 14/17, and moderately expressed in 3/17. Additionally, expression in lung squamous tumors showed high expression in 3/12 and moderate in 4/12. Contig 11 was negative for 3/4 normal lung samples, with the remaining sample having only low expression. Contig 11 showed low to moderate reactivity to salivary gland, soft palate, bladder, tonsil, skin, esophagus, and large intestine. Contig 13 (SEQ ID NO: 125) was found to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 12/17, and moderately expressed in 5/17. Contig 13 was expressed in 7/12 lung squamous tumors, with high expression in 4/12 and moderate expression in three samples. Analysis of normal lung samples showed negative expression for 2/4 and low to moderate expression in the remaining two samples. Contig 13 did show low to moderate reactivity to resting PBMC, salivary gland, bladder, pancreas, tonsil, skin, esophagus, and large intestine, as well as high expression in soft palate. Contig 16 (SEQ ID NO: 127) was found to be moderately expressed in some head and neck squamous cell tumors (6/17) and one lung squamous tumor; while showing no expression in any normal lung samples tested. Contig 16 did show low reactivity to resting PBMC, large intestine, skin, salivary gland, and soft palate. Contig 17 (SEQ ID NO: 128) was shown to be expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 5/17, and moderately expressed in 12/17. Expression levels in lung squamous tumors showed one tumor sample with high expression and 3/12 with moderate levels. Contig 17 was negative for 2/4 normal lung samples, with the remaining samples having only low expression. Additionally, low level expression was found in esophagus and soft palate. Contig 19 (SEQ ID NO: 129) was found to be expressed in most head and neck squamous cell tumors tested (11/17); with two

samples having high levels, 6/17 showing moderate expression, and low expression being found in 3/17. Testing in lung squamous tumors revealed only moderate expression in 3/12 samples. Expression levels in 2/4 of normal lung samples were negative, the two other samples having only low expression. Contig 19 showed low expression levels in esophagus, resting PBMC, salivary gland, bladder, soft palate and pancreas.

Contig 22 (SEQ ID NO: 131), was shown to be expressed in most head and neck squamous cell tumors tested (13/17) with high expression in four of these samples, moderate expression in 6/17, and low expression in 3/17. Expression levels in lung squamous tumors were found to be moderate to high for 3/12 tissues tested, with negative expression in two normal lung samples and low expression in two other samples (n=4). Contig 22 showed low expression in skin, salivary gland and soft palate. Similarly, Contig 24 (SEQ ID NO: 132) was found to be expressed in most head and neck squamous cell tumors tested (13/17) with high expression in three of these samples, moderate expression in 6/17, and low expression in 4/17. Expression levels in lung squamous tumors were found to be moderate to high for 3/12 tissues tested, with negative expression for three normal lung samples and low expression in one sample (n=4). Contig 24 showed low expression in skin, salivary gland and soft palate. Contig 29 (SEQ ID NO: 133) was expressed in nearly all head and neck squamous cell tumors tested (16/17): highly expressed in 4/17, moderately expressed in 11/17, with low expression in one sample. Also, it was moderately expressed in 3/12 lung squamous tumors, while being negative for 2/4 normal lung samples. Contig 29 showed low to moderate expression in large intestine, skin, salivary gland, pancreas, tonsil, heart and soft palate. Contig 47 (SEQ ID NO: 142) was expressed in most head and neck squamous cell tumors tested (12/17): moderate expression in 10/17, and low expression in two samples. In lung squamous tumors, it was highly expressed in one sample and moderately expressed in two others (n=13). Contig 47 was negative for 2/4 normal lung samples, with the remaining two samples having moderate expression. Also, Contig 47 showed moderate expression in large intestine, and pancreas, and low expression in skin, salivary gland, soft palate, stomach, bladder, resting PBMC, and tonsil.

Contig 48 (SEQ ID NO: 143) was expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 8/17 and moderately expressed in 7/17, with low expression in two samples. Expression levels in lung squamous tumors were high to moderate in three samples (n=13). Contig 48 was negative for one out of four normal lung samples, the remaining showing low or moderate expression. Contig 48 showed moderate expression in soft palate, large intestine, pancreas, and bladder, and low expression in esophagus, salivary gland, resting PBMC, and heart. Contig 49 (SEQ ID NO: 144) was expressed at low to moderate levels in 6/17 head and neck squamous cell tumors tested. Expression levels in lung squamous tumors were moderate in three samples (n=13). Contig 49 was negative for 2/4 normal lung samples, the remaining samples showing low expression. Moderate expression levels in skin, salivary gland, large intestine, pancreas, bladder and resting PBMC were shown, as well as low expression in soft palate, lymph nodes, and tonsil. Contig 56 (SEQ ID NO: 148) was expressed in low to moderate levels in 3/17 head and neck squamous cell tumors tested, and in lung squamous tumors, showing low to moderate levels in three out of thirteen samples. Notably, low expression levels were detected in one adenocarcinoma lung tumor sample (n=2). Contig 56 was negative for 3/4 normal lung samples, and showed moderate expression levels in only large intestine, and low expression in salivary gland, soft palate, pancreas, bladder, and resting PBMC. Contig 58, also known as L769P, (SEQ ID NO: 150) was expressed at moderate levels in 11/17 head and neck squamous cell tumors tested and low expression in one additional sample. Expression in lung squamous tumors showed low to moderate levels in three out of thirteen samples. Contig 58 was negative for 3/4 normal lung samples, with one sample having low expression. Moderate expression levels in skin, large intestine, and resting PBMC were demonstrated, as well as low expression in salivary gland, soft palate, pancreas, and bladder. Contig 59 (SEQ ID NO: 157) was expressed in some head, neck, and lung squamous tumors. Low level expression of Contig 59 was also detected in salivary gland and large intestine.

The full-length cDNA sequence for Contig 22, also referred to as L763P, is provided in SEQ ID NO: 158, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 159. Real-time RT-PCR analysis of L763P revealed

that it is highly expressed in 3/4 lung squamous tumors as well as 4/4 head and neck squamous tumors, with low level expression being observed in normal brain, skin, soft pallet and trachea. Subsequent database searches revealed that the sequence of SEQ ID NO: 158 contains a mutation, resulting in a frameshift in the corresponding protein sequence. A second cDNA sequence for L763P is provided in SEQ ID NO: 345, with the corresponding amino acid sequence being provided in SEQ ID NO: 346. The sequences of SEQ ID NO: 159 and 346 are identical with the exception of the C-terminal 33 amino acids of SEQ ID NO: 159.

The full-length cDNA sequence incorporating Contigs 17, 19, and 24, referred to as L762P, is provided in SEQ ID NO: 160, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 161. Further analysis of L762P has determined it to be a type I membrane protein and two additional variants have been sequenced. Variant 1 (SEQ ID NO: 167, with the corresponding amino acid sequence in SEQ ID NO: 169) is an alternatively spliced form of SEQ ID NO: 160 resulting in deletion of 503 nucleotides, as well as deletion of a short segment of the expressed protein. Variant 2 (SEQ ID NO: 168, with the corresponding amino acid sequence in SEQ ID NO: 170) has a two nucleotide deletion at the 3' coding region in comparison to SEQ ID NO: 160, resulting in a secreted form of the expressed protein. Real-time RT-PCR analysis of L762P revealed that is over-expressed in 3/4 lung squamous tumors and 4/4 head & neck tumors, with low level expression being observed in normal skin, soft pallet and trachea.

The full-length cDNA sequence for contig 56 (SEQ ID NO: 148), also referred to as L773P, is provided in SEQ ID NO: 171, with the predicted amino acid sequence in SEQ ID NO: 172. L773P was found to be identical to dihydroxyl dehydrogenase at the 3' portion of the gene, with divergent 5' sequence. As a result, the 69 N-terminal amino acids are unique. The cDNA sequence encoding the 69 N-terminal amino acids is provided in SEQ ID NO: 349, with the N-terminal amino acid sequence being provided in SEQ ID NO: 350. Real-time PCR revealed that L773P is highly expressed in lung squamous tumor and lung adenocarcinoma, with no detectable expression in normal tissues. Subsequent Northern blot analysis of L773P demonstrated that this transcript is differentially over-expressed in squamous tumors

and detected at approximately 1.6 Kb in primary lung tumor tissue and approximately 1.3 Kb in primary head and neck tumor tissue.

Subsequent microarray analysis has shown Contig 58, also referred to as L769S (SEQ ID NO: 150), to be overexpressed in breast tumors in addition to lung squamous tumors.

EXAMPLE 4 SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

EXAMPLE 5 PREPARATION OF ANTIBODIES AGAINST LUNG CANCER ANTIGENS

Polyclonal antibodies against the lung cancer antigens L514S, L528S and L531S (SEQ ID NO: 155, 225 and 112, respectively) were prepared as follows.

Rabbits were immunized with recombinant protein expressed in and purified from *E. coli* as described above. For the initial immunization, 400 µg of

antigen combined with muramyl dipeptide (MDP) was injected subcutaneously (S.C.). Animals were boosted S.C. 4 weeks later with 200 µg of antigen mixed with incomplete Freund's Adjuvant (IFA). Subsequent boosts of 100 µg of antigen mixed with IFA were injected S.C. as necessary to induce high antibody titer responses. Serum bleeds from immunized rabbits were tested for antigen-specific reactivity using ELISA assays with purified protein. Polyclonal antibodies against L514S, L528S and L531S were affinity purified from high titer polyclonal sera using purified protein attached to a solid support.

Immunohistochemical analysis using polyclonal antibodies against L514S was performed on a panel of 5 lung tumor samples, 5 normal lung tissue samples and normal colon, kidney, liver, brain and bone marrow. Specifically, tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with antibody for 1 hr. HRP-labeled anti-mouse followed by incubation with DAB chromogen was used to visualize L514S immunoreactivity. L514S was found to be highly expressed in lung tumor tissue with little or no expression being observed in normal lung, brain or bone marrow. Light staining was observed in colon and kidney. Staining was seen in normal liver but no mRNA has been detected in this tissue making this result suspect.

EXAMPLE 6

PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

Immunogenic peptides from the lung cancer antigen L762P (SEQ ID NO: 161) for HLA-A2/K^b-restricted CD8⁺ T cells were identified as follows.

The location of HLA-A2 binding peptides within the lung cancer antigen L762P (SEQ ID NO: 161) was predicted using a computer program which predicts peptides sequences likely to be to HLA-A*0201 by fitting to the known peptide binding motif for HLA-A*0201 (Rupert *et al.* (1993) *Cell* 74:929; Rammensee *et al.* (1995) *Immunogenetics* 41:178-228). A series of 19 synthetic peptides corresponding to a selected subset of the predicted HLA-A*0201 binding peptides was prepared as described above.

Mice expressing the transgene for human HLA A2/K^b (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with the synthetic peptides, as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 50µg of L726P peptide and 120µg of an I-A^b binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared. Cells were then resuspended at 7×10^6 cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2×10^{-5} M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) L762P peptide- (5µg/ml) and 10mg/ml B₂-microglobulin- (3 µg/ml) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). After six days, cells (5×10^5 /ml) were restimulated with 2.5×10^6 /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and 5×10^6 /ml irradiated (3000 rads) A2/K^b-transgenic spleen feeder cells. Cells were cultured in the presence of 10U/ml IL-2. Cells were restimulated on a weekly basis as described, in preparation for cloning the line.

Peptide-specific cell lines were cloned by limiting dilution analysis with irradiated (20,000 rads) L762P peptide-pulsed EL4 A2Kb tumor cells (1×10^4 cells/well) as stimulators and irradiated (3000 rads) A2/K^b-transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 10U/ml IL-2. On day 7, cells were restimulated as before. On day 14, clones that were growing were isolated and maintained in culture.

Cell lines specific for L762P-87 (SEQ ID NO: 226; corresponding to amino acids 87-95 of SEQ ID NO: 161), L726P-145 (SEQ ID NO: 227; corresponding to amino acids 145-153 of SEQ ID NO: 161), L726P-585 (SEQ ID NO: 228; corresponding to amino acids 585-593 of SEQ ID NO: 161), L762P-425 (SEQ ID NO: 229; corresponding to amino acids 425-433 of SEQ ID NO: 161), L762P(10)-424 (SEQ ID NO: 230; corresponding to amino acids 424-433 of SEQ ID NO: 161) and L762P(10)-458 (SEQ ID NO: 231; corresponding to amino acids 458-467 of SEQ ID

NO: 161) demonstrated significantly higher reactivity (as measured by percent specific lysis) against L762P peptide-pulsed EL4-A2/K^b tumor target cells than control peptide-pulsed EL4-A2/K^b tumor target cells.

5

EXAMPLE 7

IDENTIFICATION OF CD4 IMMUNOGENIC T CELL EPITOPES DERIVED
FROM THE LUNG CANCER ANTIGEN L762P

CD4 T cell lines specific for the antigen L762P (SEQ ID NO: 161) were
10 generated as follows.

A series of 28 overlapping peptides were synthesized that spanned approximately 50% of the L762P sequence. For priming, peptides were combined into pools of 4-5 peptides, pulsed at 20 micrograms/ml into dendritic cells for 24 hours. The dendritic cells were then washed and mixed with positively selected CD4⁺ T cells in 96
15 well U-bottomed plates. Forty cultures were generated for each peptide pool. Cultures were restimulated weekly with fresh dendritic cells loaded with peptide pools. Following a total of 3 stimulation cycles, cells were rested for an additional week and tested for specificity to antigen presenting cells (APC) pulsed with peptide pools using interferon-gamma ELISA and proliferation assays. For these assays, adherent
20 monocytes loaded with either the relevant peptide pool or an irrelevant peptide were used as APC. T cell lines that appeared to specifically recognize L762P peptide pools both by cytokine release and proliferation were identified for each pool. Emphasis was placed on identifying T cells with proliferative responses. T cell lines that demonstrated either both L762P-specific cytokine secretion and proliferation, or strong proliferation
25 alone were further expanded to be tested for recognition of individual peptides from the pools, as well as for recognition of recombinant L762P. The source of recombinant L762P was *E. coli*, and the material was partially purified and endotoxin positive. These studies employed 10 micrograms of individual peptides, 10 or 2 micrograms of an irrelevant peptide, and 2 or 0.5 micrograms of either L762P protein or an irrelevant,
30 equally impure, *E. coli* generated recombinant protein. Significant interferon-gamma production and CD4 T cell proliferation was induced by a number of L762P-derived

peptides in each pool. The amino acid sequences for these peptides are provided in SEQ ID NO: 232-251. These peptides correspond to amino acids 661-680, 676-696, 526-545, 874-893, 811-830, 871-891, 856-875, 826-845, 795-815, 736-755, 706-725, 706-725, 691-710, 601-620, 571-590, 556-575, 616-635, 646-665, 631-650, 541-560
5 and 586-605, respectively, of SEQ ID NO: 161.

CD4 T cell lines that demonstrated specificity for individual L762P-derived peptides were further expanded by stimulation with the relevant peptide at 10 micrograms/ml. Two weeks post-stimulation, T cell lines were tested using both proliferation and IFN-gamma ELISA assays for recognition of the specific peptide. A
10 number of previously identified T cells continued to demonstrate L762P-peptide specific activity. Each of these lines was further expanded on the relevant peptide and, following two weeks of expansion, tested for specific recognition of the L762P-peptide in titration experiments, as well as for recognition of recombinant *E. coli*-derived L762P protein. For these experiments, autologous adherent monocytes were pulsed with either
15 the relevant L762P-derived peptide, an irrelevant mammaglobin-derived peptide, recombinant *E. coli*-derived L762P (approx. 50% pure), or an irrelevant *E. coli*-derived protein. The majority of T cell lines were found to show low affinity for the relevant peptide, since specific proliferation and IFN-gamma ratios dramatically decreased as L762P peptide was diluted. However, four lines were identified that demonstrated
20 significant activity even at 0.1 micrograms/ml peptide. Each of these lines (referred to as A/D5, D/F5, E/A7 and E/B6) also appeared to specifically proliferate in response to the *E. coli*-derived L762P protein preparation, but not in response to the irrelevant protein preparation. The amino acid sequences of the L762P-derived peptides recognized by these lines are provided in SEQ ID NO: 234, 249, 236 and 245,
25 respectively. No protein specific IFN-gamma was detected for any of the lines. Lines A/D5, E/A7 and E/B6 were cloned on autologous adherent monocytes pulsed with the relevant peptide at 0.1 (A/D5 and E/A7) or 1 (D/F5) microgram/ml. Following growth, clones were tested for specificity for the relevant peptide. Numerous clones specific for the relevant peptide were identified for lines A/D5 and E/A7.

EXAMPLE 8
PROTEIN EXPRESSION OF LUNG TUMOR-SPECIFIC ANTIGENS

5 a) Expression of L514S in *E. coli*

 The lung tumor antigen L514S (SEQ ID NO: 89) was subcloned into the expression vector pE32b at NcoI and NotI sites, and transformed into *E. coli* using standard techniques. The protein was expressed from residues 3-153 of SEQ ID NO: 89. The expressed amino acid sequence and the corresponding DNA sequence are
10 provided in SEQ ID NO: 252 and 253, respectively.

 b) Expression of L762P

 Amino acids 32-944 of the lung tumor antigen L762P (SEQ ID NO: 161), with a 6X His Tag, were subcloned into a modified pET28 expression vector,
15 using kanamycin resistance, and transformed into BL21 CodonPlus using standard techniques. Low to moderate levels of expression were observed. The determined DNA sequence of the L762P expression construct is provided in SEQ ID NO: 254.

 From the foregoing it will be appreciated that, although specific
20 embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

CLAIMS

1. An isolated polypeptide, comprising at least an
5 immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor
protein comprises an amino acid sequence that is encoded by a polynucleotide sequence
selected from the group consisting of:

(a) sequences recited in SEQ ID NO: 1-3, 6-8, 10-13, 15-
27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78,
10 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133,
142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175,
179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214,
217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-
281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317,
15 323, 345, 347 and 349;

(b) sequences that hybridize to a sequence recited in any
one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52,
54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109,
111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154,
20 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191,
193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258,
260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295,
296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 under
moderately stringent conditions; and

25 (c) complements of sequences of (a) or (b).

2. An isolated polypeptide according to claim 1,
wherein the polypeptide comprises an amino acid sequence that is encoded by a
polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29,
30 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-
109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158,

160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a complement of any of the foregoing polynucleotide sequences.

5

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 110, 112, 114, 152, 155, 156, 159, 161, 165, 166, 169, 170, 172, 174, 176, 226-252, 346, 348 and 350.

4. An isolated polynucleotide encoding at least 15 amino acid
10 residues of a lung tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29,
15 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a
20 complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO:
25 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317,
30 323, 345, 347 and 349 or a complement of any of the foregoing sequences.

6. An isolated polynucleotide, comprising a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349.

7. An isolated polynucleotide, comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349_ under moderately stringent conditions.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector, comprising a polynucleotide according to any one of claims claim 4-8.

10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a lung tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84,

86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and
5 349_ or a complement of any of the foregoing polynucleotide sequences.

12. A fusion protein, comprising at least one polypeptide according to claim 1.

10 13. A fusion protein according to claim 12, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

14. A fusion protein according to claim 12, wherein the fusion
15 protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

15. A fusion protein according to claim 12, wherein the fusion protein comprises an affinity tag.

20

16. An isolated polynucleotide encoding a fusion protein according to claim 12.

17. A pharmaceutical composition, comprising a physiologically
25 acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- 30 (e) a polynucleotide according to claim 16.

18. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.

19. A vaccine according to claim 18, wherein the immunostimulant is an adjuvant.

20. A vaccine according to any claim 18, wherein the immunostimulant induces a predominantly Type I response.

21. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 17.

22. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 18.

23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.

25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

5 (a) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171,
10 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(c) complements of sequences of (i) or (ii);
in combination with an immunostimulant.

15 26. A vaccine according to claim 25, wherein the immunostimulant is an adjuvant.

27. A vaccine according to claim 25, wherein the immunostimulant induces a predominantly Type I response.

20

28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

29. A method for inhibiting the development of a cancer in a patient,
25 comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

30 (a) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and

349;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(c) complements of sequences of (i) or (ii) encoded by a polynucleotide recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349; and thereby inhibiting the development of a cancer in the patient.

30. A method according to claim 29, wherein the antigen-presenting cell is a dendritic cell.

31. A method according to any one of claims 21, 22 and 29, wherein the cancer is lung cancer.

32. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349; and

(ii) complements of the foregoing polynucleotides; wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the antigen from the sample.

33. A method according to claim 32, wherein the biological sample is blood or a fraction thereof.

34. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 32.

5

35. A method for stimulating and/or expanding T cells specific for a lung tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

(a) polypeptides comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(ii) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(iii) complements of sequences of (i) or (ii);

(b) polynucleotides encoding a polypeptide of (a); and

(c) antigen presenting cells that express a polypeptide of (a);

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

25

36. An isolated T cell population, comprising T cells prepared according to the method of claim 35.

37. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 36.

30

38. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient
5 with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

10 (1) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(2) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158,
15 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(3) complements of sequences of (1) or (2);

(ii) polynucleotides encoding a polypeptide of (i); and

(iii) antigen presenting cells that expresses a polypeptide of
20 (i);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

25 39. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion
30 of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence

selected from the group consisting of:

(1) sequences recited in SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349;

(2) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 under moderately stringent conditions; and

(3) complements of sequences of (1) or (2);

(ii) polynucleotides encoding a polypeptide of (i); and

(iii) antigen presenting cells that express a polypeptide of (i); such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells;

and

(c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

40. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with a binding agent that binds to a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

(c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

41. A method according to claim 40, wherein the binding agent is an

antibody.

42. A method according to claim 43, wherein the antibody is a monoclonal antibody.

5

43. A method according to claim 40, wherein the cancer is lung cancer.

44. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347 and 349 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

45. A method according to claim 44, wherein the binding agent is an antibody.

46. A method according to claim 45, wherein the antibody is a monoclonal antibody.

30

47. A method according to claim 44, wherein the cancer is a lung

cancer.

48. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

5 (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347
10 and 349 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the
15 presence or absence of a cancer in the patient.

49. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

20

50. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

25 51. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a
30 polynucleotide sequence recited in any one of SEQ ID NO: 1-109, 111, 113, 115-151, 153, 154, 157, 158, 160, 162-164, 167, 168, 171, 173, 175, 177-224, 255-337, 345, 347

and 349 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained
5 from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

10 52. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

53. A method according to claim 51, wherein the amount of
15 polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

54. A diagnostic kit, comprising:

(a) one or more antibodies according to claim 11; and
20 (b) a detection reagent comprising a reporter group.

55. A kit according to claim 54, wherein the antibodies are immobilized on a solid support.

25 56. A kit according to claim 54, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

57. A kit according to claim 54, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent
30 groups, enzymes, biotin and dye particles.

58. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a lung tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349 or a complement of any of the foregoing polynucleotides.

59. A oligonucleotide according to claim 58, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO: 1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 173, 175, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253, 254-258, 260, 262-264, 270, 272, 275, 276, 279-281, 286, 287, 291, 293, 295, 296, 300, 302, 308-310, 313, 315-317, 323, 345, 347 and 349.

60. A diagnostic kit, comprising:
(a) an oligonucleotide according to claim 59; and
(b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

SEQUENCE LISTING

<110> Corixa Corporation et al.

<120> COMPOUNDS AND METHODS FOR THERAPY
AND DIAGNOSIS OF LUNG CANCER

<130> 210121.45501PC

<140> PCT

<141> 2000-04-03

<160> 350

<170> FastSEQ for Windows Version 3.0

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gcagagacag	actggtggtt	gaacctggag	gtgccaaaaa	agccagctgc	gggccagga	60
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ttcatctcca	gcagagacaa	cggaggaggc	tcccaccagg	acggttctca	ttatttatat	180
gttaatatgt	ttgtaaactc	atgtacagtt	ttttttgggg	gggaagcaat	gggaanggta	240
naaattacaa	atagaatcat	ttgctgtaat	ccttaaatgg	caaacggtca	ggccacgtga	300
aaaaaaaaaa	aaaaa					315

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<211> 380

<212> DNA

<213> Homo sapien

<400> 2

atttaggctt	aagattttgt	ttacccttgt	tactaaggag	caaattagta	ttaaagtata	60
atatatataa	acaaatacaa	aaagttttga	gtggttcagc	ttttttatatt	tttttaattg	120
cataactttt	aacaacactg	ctctgtaatg	ggttgaactg	tggtactcag	actgagataa	180
ctgaaatgag	tggtatgtata	gtgttattgc	ataattatcc	cactatgaag	caaagggact	240
ggataaattc	ccagtctaga	ttattagcct	ttgttaacca	tcaagcacct	agaagaagaa	300
ttattggaaa	ttttgtcttc	tgtaactggc	actttggggg	gtgacttata	ttttgccttt	360
gtaaaaaaaa	aaaaaaaaaa					380

<210> 3

<211> 346

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<220>
 <221> misc_feature
 <222> (1)...(346)
 <223> n = A,T,C or G

<400> 3
 ttgtaagtat acaatttttag aaaggattaa atgttattga tcattttact gaatactgca 60
 catcctcacc atacaccatc cactttccaa taacatttaa tcctttctaa aattgtaagt 120
 atacaattgt actttctttg gattttcata acaaataac catagactgt taattttatt 180
 gaagtttcct taatggaatg agtcattttt gtcttgtgct tttgagggtta cctttgcttt 240
 gacttccaac aatttgatca tatagtgttg agctgtggaa atctttaagt ttattctata 300
 gcaataattt ctattnnnag annccnggnn naaaannann annaaa 346

<210> 4
 <211> 372
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(372)
 <223> n = A,T,C or G

<400> 4
 actagtctca ttactccaga attatgctct tgtacctgtg tggctgggtt tcttagtcgt 60
 tggtttgggtt tggttttttg aactgggatg taggggtggtt cacagttcta atgtaagcac 120
 tctcttctcc aagtgtgtgt ttgtggggac aatcattctt tgaacattag agaggaaggc 180
 agttcaagct gttgaaaaga ctattgctta tttttgtttt taaagacctt cttgacgtca 240
 tgtggacagt gcacgtgcct tacgctacat cttgttttct aggaagaagg ggatgcnggg 300
 aaggantggg tgctttgtga tggataaaac gnctaaataa cacacctta cattttgaaa 360
 aaaacaaaac aa 372

<210> 5
 <211> 698
 <212> DNA
 <213> Homo sapien

<220>
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 <222> (1)...(698)
 <223> n = A,T,C or G

<400> 5
 actagtanga tagaaacact gtgtcccgag agtaaggaga gaagctacta ttgattagag 60
 cctaaccag gtttaactgca agaagaggcg ggatactttc agctttccat gtaactgtat 120
 gcataaagcc aatgtagtcc agtttctaag atcatgttcc aagctaactg aatcccactt 180
 caatacacac tcatgaactc ctgatggaac aataacaggc ccaagcctgt ggtatgatgt 240
 gcacacttgc tagactcaga aaaaatacta ctctcataaa tgggtgggag tattttgggt 300
 gacaacctac ttgtcttggc tgagtgaagg aatgatattc atatnttcat ttattccatg 360
 gacatttagt tagtgctttt tatataccag gcatgatgct gagtgacact cttgtgtata 420
 tntccaaatn ttngtnngt cgctgcacat atctgaaatc ctatattaag antttcccaa 480
 natgangtcc ctgggtttttc cagccactt gatcngtcaa ngatctcacc tctgtntgtc 540
 ctaaaaccnt ctncnngg gttagaacngg acctctcttc tcccttcccg aanaatnaag 600
 tgtgngaaga nanccnncn cccctctnnc tncnncctng ccngctnnnc cncntgtngg 660

gggngccgcc cccgcggggg gacccccccn ttttcccc

698

<210> 6
 <211> 740
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(740)
 <223> n = A,T,C or G

<400> 6
 actagtcaaa aatgctaaaa taatttggga gaaaatattt ttttaagtagt gttatagttt 60
 catgtttatc ttttattatg tnttgtgaag ttgtgtcttt tcactaatta cctatactat 120
 gccaatattt ccttataatc atccataaca ttatactac atttgtaaga gaatatgcac 180
 gtgaaactta acactttata aggtaaaaat gaggtttcca agatttaata atctgatcaa 240
 gttcttggtt ttcccaaata gaatggactt ggtctgttaa ggggctaagg gagaagaaga 300
 agataagggt aaaagtgtgt aatgaccaa cattctaaaa gaaatgcaa aaaaaattta 360
 ttttcaagcc ttcgaactat ttaaggaaa caaaatcatt tcctanatgc atatcatttg 420
 tgagantttc tcantaatat cctgaatcat tcatttcagc tnaggcttca tgttgactcg 480
 atatgtcatc tagggaaagt ctatttcatt gtccaaacct gttgccatag ttggttaggc 540
 tttcctttta ntgtgaanta ttnacangaa attttctctt tnanagttct tnatagggtt 600
 aggggtgtgg gaaaagcttc taacaatctg tagtgtnncc tggtatctgt ncagaaccan 660
 aatnacggat cgnangaagg actgggtcta tttacangaa cgaatnatct ngttnnntgt 720
 gttnnncaact ccngggagcc 740

<210> 7
 <211> 670
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(670)
 <223> n = A,T,C or G

<400> 7
 gctgggggagc tcggcatggc ggtccccgct gcagccatgg ggccctcggc gttggggccag 60
 agcggccccc gctcgatggc cccgtggtgc tcagtgaaga gcggcccgtc gcgctacgtg 120
 cttgggatgc aggagctgtt ccggggccac agcaagaccg cgagttcctg gcgcacagcg 180
 ccaagggtgca ctccgtggcc tggagtgtgc acgggcgtcg cctacctcgg ggtcttcgac 240
 aagacgccac gtcttcttgc tgganaanga ccgttgggtca aagaaaacaa ttatcgggga 300
 catgggggata gtgtggacca ctttgttggc atccaagtaa tcctgacctt tttgttacgg 360
 cgtctggaga taaaaccatt cgcactctgg atgtgaggac tacaaaatgc attgccactg 420
 tgaacactaa aggggagaac attaatatct gctggantcc tgatgggcan accattgctg 480
 tagcnacaag gatgatgtgg tgactttatt gatgccaaga aaccccggtc caaagcaaaa 540
 aaacanttcc aanttcgaag tcacnnaaat ctctggaac aatgaacatn aatatnttct 600
 tcctgacaat ggnccctggg tgnntccat cctcagctnc cccaaaactg aancctgtnc 660
 natccacccc 670

<210> 8
 <211> 689
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (689)
 <223> n = A,T,C or G

<400> 8

actagtatct	aggaatgaac	agtaaaagag	gagcagttgg	ctacttgatt	acaacagagt	60
aaatgaagta	ctggatttgg	gaaaacctgg	ttttattaga	acatatggaa	tgaaagccta	120
cacctagcat	tgccacttta	gccccctgaa	ttaacagagc	ccaattgaga	caaaccctg	180
gcaacaggaa	attcaaggga	gaaaaagtaa	gcaacttggg	ctaggatgag	ctgactccct	240
tagagcaaag	ganagacagc	ccccattacc	aaataccatt	tttgccctggg	gcttgtgcag	300
ctggcagtg	tcctgcccc	gcatggcacc	ttatngtttt	gatagcaact	tcgttgaatt	360
ttcaccaact	tattacttga	aattataata	tagcctgtcc	gtttgctgt	tcagggtgt	420
gatatatntt	cctagtgggt	tgacttttnaa	aataaatnag	gtttantttt	ctccccenn	480
cnntnctncc	nntnctenn	cnntcccccc	cnctcngtcc	tcnnnnnttn	gggggggcn	540
ccccnccgn	ggacccccct	ttggtccctt	agtggagggt	natggcccc	ggnttatcc	600
nggcctann	tttccccgtn	nnaaatgntt	ccccctccca	ntccnccac	ctcaanccgg	660
aagcctaagt	ttntaccctg	gggggtcccc				689

<210> 9
 <211> 674
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (674)
 <223> n = A,T,C or G

<400> 9

gtccactctc	ctttgagtg	actgtcttac	tgtgcactct	gtttttcaac	tttctagata	60
taaaaaatgc	ttgttctata	gtggagtaag	agctcacaca	cccaaggcag	caagataact	120
gaaaaaagcg	aggctttttt	gccaccctgg	taaaggccag	ttcactgcta	tagaactgct	180
ataagcctga	aggggaagtag	ctatgagact	ttccattttt	cttagttctc	ccaataggct	240
ccttcatgga	aaaaggcttc	ctgtaataat	tttcacctaa	tgaattagca	gtgtgattat	300
ttctgaaata	agagacaaat	tgggcccgag	agtcttctctg	tgatttaaaa	taaacaaccc	360
aaagttttgt	ttggtcttca	ccaaaggaca	tactctaggg	ggtatgttgt	tgaagacatt	420
caaaaacatt	agctgttctg	tctttcaatt	tcaagttatt	ttggagactg	cctccatgtg	480
agttaattac	tttgctctgg	aactagcatt	attgtcatta	tcacacatt	ctgtcatcat	540
catctgaata	atattgtgga	tttccccctc	tgcttgcac	ttcttttgac	tcctctggga	600
anaaatgtca	aaaaaaaagg	tcgatctact	cngcaaggnc	catctaata	ctgcgctgga	660
aggaccnct	gccc					674

<210> 10
 <211> 346
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (346)
 <223> n = A,T,C or G

<400> 10

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actagtctgc tgatagaaag cactatacat cctattgttt ctttctttcc aaaatcagcc      60
ttctgtctgt aacaaaaatg tactttatag agatggagga aaaggtctaa tactacatag      120
ccttaagtgt ttctgtcatt gttcaagtgt attttctgta acagaaacat atttggaatg      180
tttttctttt ccccttataa attgtaattc ctgaaatact gctgctttaa aaagtccac      240
tgtcagatta tattatctaa caattgaata ttgtaaatat acttgtctta cctctcaata      300
aaagggact tttctattan nnagnngnnn gnnnnataaa anaaaa      346

```

```

<210> 11
<211> 602
<212> DNA
<213> Homo sapien

```

```

<400> 11
actagtaaaa agcagcattg ccaaataatc cctaattttc cactaaaaat ataatgaaat      60
gatgttaagc tttttgaaaa gtttaggtta aacctactgt tgtagatta atgtatttgt      120
tgcttccctt tatctggaat gtggcattag cttttttatt ttaaccctct ttaattctta      180
ttcaattcca tgacttaagg ttggagagct aaacactggg atttttggat aacagactga      240
cagttttgca taattataat cggcattgta catagaaagg atatggctac cttttgttaa      300
atctgcactt tctaaatata aaaaaaggga aatgaagtta taaatcaatt tttgtataat      360
ctgtttgaaa catgagtttt atttgcttaa tattagggtt ttgccccctt tctgtaagtc      420
tcttgggatc ctgtgtagaa ctgttctcat taaacaccaa acagttaagt ccattctctg      480
gtactagcta caaattcggg ttcatattct acttaacaat ttaaataaac tgaaatatatt      540
ctagatgggc tacttctgtt catataaaaa caaaacttga tttccaaaaa aaaaaaaaaa      600
aa                                                                                   602

```

```

<210> 12
<211> 685
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(685)
<223> n = A,T,C or G

```

```

<400> 12
actagtcctg tgaaagtaca actgaaggca gaaagtgtta ggattttgca tctaattgttc      60
attatcatgg tattgatgga cctaagaaaa taaaaattag actaagcccc caaataagct      120
gcatgcattt gtaacatgat tagtagattt gaatatatag atgtagtatn ttgggtatct      180
aggtgtttta tcattatgta aaggaattaa agtaaaggac tttgtagttg tttttattaa      240
atatgcatat agtagagtgc aaaaatatag caaaaatana aactaaaggt agaaaagcat      300
tttagatatg ccttaatnta nnaactgtgc caggtggccc tcggaataga tgccaggcag      360
agaccagtgc ctgggtggtg cctccccttg tetgcccccc tgaagaactt ccctcacgtg      420
angtagtgcc ctctgtagtg tcacgtggan tantggganc aggccgnncn gtnanaagaa      480
ancanngtga nagtttcncc gtngangcng aactgtccct gngccnnnac gctcccanaa      540
cntntccaat ngacaatcga gtttccnnnc tcnngnaacc tngccgnnnn cnngeccnnc      600
cantntgnta accccgcgcc cggatcgctc tcnnttcgtt ctncncnaa ngggntttcn      660
cnnccgcccgt cncnnccccg cnncc                                                                                   685

```

```

<210> 13
<211> 694
<212> DNA
<213> Homo sapien

```

```

<220>

```

<221> misc_feature
 <222> (1)...(694)
 <223> n = A,T,C or G

<400> 13
 cactagtcac tcattagcgt tttcaatagg gctcttaagt ccagtagatt acgggtagtc 60
 agttgacgaa gatctggttt acaagaacta attaaatggt tcattgcatt tttgtaagaa 120
 cagaataatt ttataaaatg tttgtagttt ataattgccg aaaataattt aaagacactt 180
 tttctctgtg tgtgcaaatg tgtgtttgtg atccattttt tttttttttt taggacacct 240
 gtttactagc tagctttaca atatgccaaa aaaggatttc tccctgacct catccgtggt 300
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 cattggccat ggaaacagcc gangtggttg gagccagcag tgcattggc cgtccggcat 540
 ctggcntgat tggctctggc gccgtcattg tcagcacagt gccatgggac atggggaana 600
 ctgactgcac ngccaatggt tttcatgaag aatacngcat ncnngtgat cacgtnance 660
 angacgctat gggggncana gggccantt gcttc 694

<210> 14
 <211> 679
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(679)
 <223> n = A,T,C or G

<400> 14
 cagccgectg catctgtatc cagcgccang tcccgcagc cccagctgcg cgcgcccccc 60
 agtcccgnac ccgttcggcc cangctnagt tagncctcac catnccggc aaaggangca 120
 ccaagtgcac caaataacct cngtncggat nttaaattcat cttctggctt gccgggattg 180
 ctgtccntgc catgggacta nggctccgat ncgactctca gaccanganc atcttcganc 240
 naganactaa tnatnattnt tccagcttct acacaggagt ctatattctg atcggatccg 300
 gcnccctcnt gatgctggtg ggcttctctga gctgctgcgg ggctgtgcaa gagtcccant 360
 gcatgctggg actgttcttc ggcttctctt tgggtgatatn cgccattgaa atacctgcgg 420
 ccatctgggg atattccact ncatnatgt gattaaggaa ntccacggag ttttacaagg 480
 acacgtacaa cnacctgaaa accnnggatg anccccaccg ggaancnctg aangecatcc 540
 actatgcgtt gaactgcaat ggtttggtctg gggnccttga acaatttaat cncatacatc 600
 tggccccann aaaggacntn ctcgannctt tcnccgtgna attcngttct gatnccatca 660
 cagaagtctc gaacaatcc 679

<210> 15
 <211> 695
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(695)
 <223> n = A,T,C or G

<400> 15
 actagtggat aaaggccagg gatgctgctc aacctcctac catgtacagg gacgtctccc 60
 cattacaact acccaatccg aagtgtcaac tgtgtcagga ctaanaaacc ctgggtttga 120

ttaaaaaagg	gcttgaaaaa	aggggagcca	caaattctgtc	tgttctctca	cnttantcnt	180
tggcaaatna	gcattctgtc	tcnttggtctg	cngcctcanc	ncaaaaaanc	ngaactcnat	240
cngggccagg	aatacatctc	ncaatnaacn	aaattganca	aggcnntggg	aaatgccnga	300
tgggattatc	ntccgcttgt	tgancttcta	agtttcttctc	ccttcattcn	accctgccag	360
ccnagttctg	ttagaaaaat	gccngaattc	naacnccggt	tttctactc	ngaattttaga	420
tctncanaaa	cttctctggcc	acnattcnaa	ttnanggnca	cgnacanatn	ccttccatna	480
ancncacccc	acntttgana	gccangacaa	tgactgcntn	aantgaaggc	ntgaaggaan	540
aactttgaaa	ggaaaaaaa	ctttgtttcc	ggccccttcc	aacncttctg	tgtnnancac	600
tgccttctng	naaccctgga	agcccngnga	cagtgttaca	tggtgttcta	nnaaacngac	660
ncttnaatnt	cnatcttccc	nanaacgatt	ncncc			695

<210> 16

<211> 669

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(669)

<223> n = A,T,C or G

<400> 16

cgccgaagca	gcagcgcagg	ttgtccccgt	ttccccctccc	ccttcccttc	tcgggttgcc	60
ttccccgggccc	ccttacactc	cacagtccccg	gtccccgccat	gtcccagaaa	caagaagaag	120
agaaccctgc	ggaggagacc	ggcgaggaga	agcaggacac	gcaggagaaa	gaagggtattc	180
tgcctgagag	agctgaagag	gcaaagctaa	aggccaaata	cccaagccta	ggacaaaagc	240
ctggaggctc	cgacttctc	atgaagagac	tccagaaagg	gcaaaagtac	tttgactcng	300
gagactacaa	catggccaaa	gccaacatga	agaataagca	gctgccaaagt	gcangaccag	360
acaagaacct	ggtgactggt	gatcacatcc	ccacccca	ggatctgccc	agagaaagtc	420
ctcgtctgtc	accagcaagc	ttgcggttg	ccaagttgaa	tgatgctgcc	ggggctctgc	480
canatctgag	acgttccct	ccttgcceca	cccgggtcct	gtgctggctc	ctgccccttc	540
tgcttttgca	gccangggtc	aggaagtggc	ncnggtngtg	gctggaaagc	aaaacccttt	600
cctgttggtg	tcccacccat	ggagccccg	ggcgagccc	angaacttga	ncctttttgt	660
tntcttncc						695

<210> 17

<211> 697

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(697)

<223> n = A,T,C or G

<400> 17

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gacgcgtga	ggagannnac	gctggcccan	ctgccggcca	cacacgggga	tcntggtnat	120
gcctgccc	gggancccca	ncnctcgan	cccatntcac	acccgnncn	tngeccacn	180
ncctggtcn	cnngcccng	nccagctcnc	gnccccctcc	gccnnnctcn	ttnnctctc	240
cncnccctcc	ncnacacct	cctaccncg	getccctccc	cagccccccc	ccgcaancct	300
ccacnacncc	ntcnnncga	ancncnctc	genctengcc	ccngccccct	gccccccgcc	360
cncnacnncg	cgntcccccg	cgncgcngc	ctnccccct	cccacnacag	ncncaccgcg	420
agncagcnc	tccgcccnc	gacgcccnn	cccgcgcgc	tcaccttcat	ggncnncng	480
ccccgctcnc	ncnctgcnc	gccgncnng	cgcgcgcgc	cnnccgngtn	ccnncngnng	540

```

ccccngcngn angcngtgcg cnnrangnec gngccgngnn ncaccctccg nccnccgccc      600
cgcccgtggtg gggctcccg cncgcggntc antcccncc cntncccca ctntccgntc      660
cnnnctcnc gctengegen cgcccnccnc cccccc                                697

```

<210> 18

<211> 670

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(670)

<223> n = A,T,C or G

<400> 18

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ctcgtgtgaa ggggtgcagta cctaagccgg agcggggtag aggcggggccg gcacccccctt      60
ctgacctcca gtgccgccgg cctcaagatc agacatggcc cagaacttga acgacttggc      120
gggacggctg cccgccgggc cccggggcat gggcacggcc ctgaagctgt tgctgggggc      180
cggcgccgtg gcctacgggtg tgcgcgaatc tgtgttcacc gtggaaggcg ggcncagagc      240
catcttcttc aatcggtatg gtggagtgc caggacacta tcctggggccg anggccttca      300
cttcaggatc cttgggttcca gtaccccanc atctatgaca ttcggggccag acctcgaaaa      360
aatctcctcc ctacaggctc caaagaccta cagatggtga atatctccct gcgagtgttg      420
tctcgaccaa tgctcangaa ctctctaaca tgttccancg cctaagggtc ggactacnaa      480
gaacgantgt tgccgtccat tgtcacgaag tgctcaagaa tttnggtggc caagttcaat      540
gncctcacnn ctgatcnccc agcggggcca agttancct ggttgatccc cgggganctg      600
acnnaaaagg gccaaaggact tccctcctc ctggataatg tggccntcac aaagctcaac      660
tttanccacc                                670

```

<210> 19

<211> 606

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(606)

<223> n = A,T,C or G

<400> 19

```

actagtgcc aacctagctc ccaggccagt tctctgaatg tgcaggagtt ccaggatctc      60
tggcctcagt tgtccttggt tattgatggg ggacaaattg gggatggcca gagccccgag      120
tgtcgccctg gctcaactgt ggttgatttg tctgtgcccg gaaagtttgg catcattcgt      180
ccaggctgtg ccttgaaaag tactacagcc atcctccaac agaagtacgg actgctcccc      240
tcacatgcgt cctacctgtg aaactctggg aagcaggaag gccaagacc tgggtgctgga      300
tactatgtgt ctgtccactg acgactgtca aggcctcatt tgcagaggcc accggagcta      360
gggcactagc ctgactttta aggcagtgtg tctttctgag cactgtagac caagcccttg      420
gagctgctgg tttagccttg cacctgggga aaggatgtat ttatttgat tttcatatat      480
cagccaaaag ctgaatggaa aagttnagaa cattcctagg tggccttatt ctaataagtt      540
tcttctgtct gttttgtttt tcaattgaaa agttattaaa taacagattt agaatttagt      600
gagacc                                606

```

<210> 20

<211> 449

<212> DNA

<213> Homo sapien


```

<400> 20
actagtaaac aacagcagca gaaacatcag tatcagcagc gtcgccagca ggagaatatg      60
cagcgccaga gccgaggaga acccccgctc cctgaggagg acctgtccaa actcttcaaa      120
ccaccacagc cgcctgccag gatggactcg ctgctcattg caggccagat aaacacttac      180
tgccagaaca tcaaggagtt cactgccccaa aacttaggca agctcttcat ggcccaggct      240
cttcaagaat acaacaacta agaaaaggaa gtttccagaa aagaagttaa catgaactct      300
tgaagtcaca ccagggaac tcttggaaga aatatatttg catattgaaa agcacagagg      360
atctcttttag tgctattgcc gattttggct ataacagtgt ctttctagcc ataataaaat      420
aaaacaaaat cttgactgct tgctcaaaa      449

```

```

<210> 21
<211> 409
<212> DNA
<213> Homo sapien

```

```

<400> 21
tatcaatcaa ctggtgaata attaaacaat gtgtggtgtg atcatacaaa ggggtaccact      60
caatgataaa aggaacaagc tgcctatatg tggaacaaca tggatgcatt tcagaaactt      120
tatgttgagt gaaagaacaa acacggagaa catactatgt gggtctcttt atgtaacatt      180
acagaaataa aaacagaggc aaccaccttt gaggcagtat ggagtgagat agactggaaa      240
aaggaaggaa ggaaactcta cgtgatgga aatgtctgtg tcttcattgg gtggtagtta      300
tgtggggata tacatttgtc aaaattttatt gaactatata ctaaagaact ctgcatttta      360
ttgggatgta aataatacct caattaaaaa gacaaaaaaa aaaaaaaaaa      409

```

```

<210> 22
<211> 649
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (649)
<223> n = A,T,C or G

```

```

<400> 22
acaattttca ttatcttaag cacattgtac atttctacag aacctgtgat tattctcgca      60
tgataaggat ggtacttgca tatggtgaat tactactgtt gacagtttcc gcagaaatcc      120
tatttctagt gaccaacatt gtggcatggc agcaaagcc aacattttgt ggaatagcag      180
caaactctaca agagaccctg gttggttttt cgttttgttt tctttgtttt tcccccttc      240
tcctgaatca gcagggatgg aangagggta gggaagttat gaattactcc ttccagtagt      300
agctctgaag tgtcacattt aatatcagtt ttttttaaac atgattctag ttnaatgtag      360
aagagagaag aaagaggaag tgttcacttt tttaatacac tgatttagaa atttgatgtc      420
ttatatcagt agttctgagg tattgatagc ttgctttatt tctgccttta cgttgacagt      480
gttgaagcag ggtgaataac taggggcata tatatttttt ttttttgtaa gctgtttcat      540
gatgttttct ttggaatttc cggataagtt caggaaaaca tctgcatgtt gttatctagt      600
ctgaagttcn tatccatctc attacaacaa aaacnccag aacggnntg      649

```

```

<210> 23
<211> 669
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature

```

<222> (1)...(669)

<223> n = A,T,C or G

<400> 23

actagtgcg	tactggctga	aatccctgca	ggaccaggaa	gagaaccagt	tcagactttg	60
tactctcagt	caccagctct	ggaattagat	aaattccttg	aagatgtcag	gaatgggagc	120
tatcctctga	cagcctttgg	gctgcctcgg	ccccagcagc	cacagcagga	ggaggtgaca	180
tcacctgtcg	tgccccctc	tgtcaagact	ccgacacctg	aaccagctga	ggaggagact	240
cgcaagggtg	tgctgatgca	gtgcaacatt	gagtcggtgg	aggagggagt	caaacaccac	300
ctgacacttc	tgctgaagtt	ggaggacaaa	ctgaaccggc	acctgagctg	tgacctgatg	360
ccaaatgaga	atatccccga	gttggcggtc	gagctggtgc	agctgggctt	cattagttag	420
gctgaccaga	gccggttgac	ttctctgcta	gaagagactt	gaacaagtgc	aattttgccca	480
ggaacagtac	cctcaactca	gccgctgtca	ccgtctcctc	ttagagctca	ctcggggccag	540
gccctgatct	gcgctgtggc	tgctctggac	gtgctgcacc	ctctgtcctt	ccccccagtc	600
agtattacct	gtgaagccct	tccctccttt	attattcagg	anggctgggg	gggctccttg	660
nttctaacc						669

<210> 24

<211> 442

<212> DNA

<213> Homo sapien

<400> 24

actagtacca	tcttgacaga	ggatacatgc	tcccaaaacg	tttgttacca	cacttaaaaa	60
tcactgccat	cattaagcat	cagtttcaaa	attatagcca	ttcatgattt	actttttcca	120
gatgactatc	attattctag	tcctttgaat	ttgtaagggg	aaaaaaaaa	aaaacaaaaa	180
cttacgatgc	acttttctcc	agcacatcag	atttcaaatt	gaaaattaaa	gacatgctat	240
ggtaatgcac	ttgctagtac	tacacacttt	ggtacaacaa	aaaacagagg	caagaaacaa	300
cggaaagaga	aaagccttcc	tttgttggcc	cttaaaactga	gtcaagatct	gaaatgtaga	360
gatgatctct	gacgatacct	gtatgttctt	attgtgtaaa	taaaattgct	ggtatgaaat	420
gacctaataa	aaaaaaaaga	aa				442

<210> 25

<211> 656

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(656)

<223> n = A,T,C or G

<400> 25

tgcaagtacc	acacactggt	tgaattttgc	acaaaaagtg	actgtaggat	cagggtgatag	60
ccccggaatg	tacagtgtct	tggtgcacca	agatgccttc	taaaggctga	cataccttgg	120
accctaattg	ggcagagagt	atagccctag	cccagtggtg	acatgaccac	tccctttggg	180
aggcctgagg	tagaggggag	tggtatgtgt	tttctcagtg	gaagcagcac	atgagtgggt	240
gacaggatgt	tagataaagg	ctctagttag	ggtgtcattg	tcatttgaga	gactgacaca	300
ctcctagcag	ctggtaaagg	ggtgctggan	gccatggagg	anctctagaa	acattagcat	360
gggctgatct	gattacttcc	tgcatcccg	ctcactttta	tgggaagtct	tattagangg	420
atgggacagt	tttccatata	cttgctgtgg	agctctggaa	cactctctaa	atttccctct	480
attaaaaatc	actgccctaa	ctacacttcc	tccttgaagg	aatagaaatg	gaactttctc	540
tgacatantt	cttggcatgg	ggagccagcc	acaaatgana	atctgaacgt	gtccagggtt	600
ctcctganac	tcactctacat	agaattgggt	aaaccctccc	ttggaataag	gaaaaa	656

<210> 26
 <211> 434
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(434)
 <223> n = A,T,C or G

<400> 26
 actagttcag actgccacgc caaccccaga aaatacccca catgccagaa aagtgaagtc 60
 ctaggtgttt ccatctatgt ttcaatctgt ccatctacca ggcctcgca taaaaacaaa 120
 acaaaaaaac gctgccaggt tttagaagca gttctggtct caaaaccatc aggatcctgc 180
 caccagggtt cttttgaaat agtaccacat gtaaaaggga atttggcttt cacttcatct 240
 aataactgaa ttgtcaggct ttgattgata attgtagaaa taagtagcct tctgttgtgg 300
 gaataagtta taatcagtat tcatctcttt gttttttgtc actcttttct ctctaattgt 360
 gtcatttgta ctgtttgaaa aatatttctt ctatnaaatt aaactaacct gccttaaaaa 420
 aaaaaaaaaa aaaa 434

<210> 27
 <211> 654
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(654)
 <223> n = A,T,C or G

<400> 27
 actagtccaa cacatgcaga aacattgttt tgaatcctct gtaaaccaag gcattaatct 60
 taataaacca ggatccattt aggtaccact tgatataaaa aggatatcca taatgaatat 120
 tttatactgc atcctttaca ttagccacta aatacgttat tgcttgatga agacctttca 180
 cagaatccta tggattgcag catttcactt ggctacttca taccatgcc ttaaagaggg 240
 gcagtttctc aaaagcagaa acatgccgcc agttctcaag ttttcctcct aactccattt 300
 gaatgtaagg gcagctggcc cccaatgtgg ggaggctcga acattttctg aattcccatt 360
 ttcttgttcg cggctaaatg acagtttctg tcattactta gattccgatc tttcccaaag 420
 gtgttgattt acaaagaggc cagctaatag cagaaatcat gaccctgaaa gagagatgaa 480
 attcaagctg tgagccaggc agganctcag tatggcaaag gtcttgagaa tcngccattt 540
 ggtacaaaaa aaatttttaa gcntttatgt tataccatgg aaccatagaa anggcaaggg 600
 aattgttaag aanaatttta agtgtccaga ccanaanga aaaaaaaaaa aaaa 654

<210> 28
 <211> 670
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(670)
 <223> n = A,T,C or G

<400> 28
 cgtgtgcaca tactgggagg atttccacag ctgcacggtc acagccctta cggattgccca 60

```

ggaaggggagc aaagatatgt gggataaact gagaaaagaa nccaaaaacc tcaacatcca 120
aggcagctta ttcgaactct gcggcagcgg caacggggcg gcgggggtccc tgctcccggc 180
gttcccgggtg ctctctgggtg ctctctcggc agcttttagcg acctgncttt ccttctgagc 240
gtggggccag cccccccgc ggcgcccacc cacnctcact ccatgctccc ggaaatcgag 300
aggaagatca ttagttcttt ggggaagttt gtgattctct gtgatgctga aaaacactca 360
tatagggaat gtgggaaatc ctganctctt tnttatntcg tntgatttct tgtgttttat 420
ttgccaaaat gttaccaatc agtgaccaac cnagcacagc caaaaatcgg acntcngctt 480
tagtccgtct tcacacacag aataagaaaa cggcaaacc accccacttt tnannttnat 540
tattactaan ttttttctgt tgggcaaaaag aatctcagga acngccctgg ggcnccgta 600
ctanagttaa ccnagctagt tncatgaaaa atgatgggct ccnctcaat gggaaagcca 660
agaaaaagnc 670

```

<210> 29

<211> 551

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(551)

<223> n = A,T,C or G

<400> 29

```

actagtcttc cacagcctgt gaatccccct agacctttca agcatagtga gcggagaaga 60
agatctcagc gtttagccac cttacccatg cctgatgatt ctgtagaaaa ggtttcttct 120
ccctctccag ccactgatgg gaaagtattc tccatcagtt ctcaaaatca gcaagaatct 180
tcagtaccag aggtgcctga tgttgacat ttgccacttg agaagctggg accctgtctc 240
cctcttgact taagtctgtg ttcagaagtt acagcaccgg tagcctcaga ttctctctac 300
cgtaatgaat gtcccagggc agaaaaagag gatacncaga tgcttccaaa tcttctctcc 360
aaagcaatag ctgatgggaa gaggagctcc agcagcagca ggaatatcga aaacagaaaa 420
aaaagtgaat ttgggaagac aaaagctcaa cagcatttgg taaggagaaa aganaagatg 480
aggaaggaag agagaagaga gacnaagatc nctacggacc gnnncggaag aagaagaagn 540
aaaaanaaaa a 551

```

<210> 30

<211> 684

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(684)

<223> n = A,T,C or G

<400> 30

```

actagttcta tctggaaaaa gcccggttg gaagaagctg tggagagtgc gtgtgcaatg 60
cgagactcat ttcttggaag catccctggc aaaaatgcag ctgagtacaa ggttatcact 120
gtgatagaac ctggactgct ttttgagata atagagatgc tgcagtctga agagacttcc 180
agcacctctc agttgaatga attaatgatg gcttctgagt caactttact ggctcaggaa 240
ccacgagaga tgactgcaga tgtaatcgag cttaaaggga aattcctcat caacttagaa 300
gggtggtgata ttcgtgaaga gtcttcttat aaagtaattg tcatgccgac tacgaaagaa 360
aaatgcccc gttgttgga gtatacagcg ggagtcttca gatacactgt gtcctcgatg 420
tgcagaagtt gtcagtggga aaatagtatt aacagctcac tcgagcaaga accctcctga 480
cagtactggg ctagaagttt ggatggatta tttacaatat aggaaagaaa gccagaatt 540
aggtnatgag tggatgagta aatggtggan gatggggaat tcaaatcaga attatggaag 600

```

aagttnttcc tgttactata gaaaggaatt atgtttatatt acatgcagaa aatatanatg 660
tgtggtgtgt accgtggatg gaan 684

<210> 31
<211> 654
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(654)
<223> n = A,T,C or G

<400> 31
gcgcagaaaa ggaaccaata tttcagaaac aagcttaata ggaacagctg cctgtacatc 60
aacatcttct cagaatgacc cagaagttat catcgtggga gctggcgtgc ttggctctgc 120
tttggcagct gtgctttcca gagatggaag aaagggtgaca gtcattgaga gagacttaaa 180
agagcctgac agaatagttg gagaattcct gcagccgggt gggtatcatg ttctcaaaga 240
ccttggtctt ggagatacag tggaaggtct tgatgccag gttgtaaagt gttacatgat 300
tcatgatcag ggaaagcaaa tcagangttc agattcetta cctctgttca gaaaacaatc 360
aagtgcagag tggaagagct ttccatcacg gaagattcat catgagtctc cggaaagcag 420
ctatggcaga gcccaatgca aagttttattg aagggtgttgt gttacagtta ttagaggaag 480
atgatgttgt gatgggagtt cagtacaagg ataaagagac tgggagatat caaggaactc 540
catgctccac tgactgttgt tgcagatggg cttttctcca anttcaggaa aagcctggtc 600
tcaataaagt ttctgtatca ctcatcttggg tggcttctta tgaagaatgc nccc 654

<210> 32
<211> 673
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(673)
<223> n = A,T,C or G

<400> 32
actagtgaag aaaaagaaat tctgatacgg gacaaaaatg ctcttcaaaa catcattctt 60
tatcacctga caccaggagt tttcattgga aaaggatttg aacctgggtg tactaacatt 120
ttaaagacca cacaaggaag caaaatcttt ctgaaagaag taaatgatac acttctgggtg 180
aatgaattga aatcaaaaaga atctgacatc atgacaacaa atgggtgtaat tcatgttgta 240
gataaactcc tctatccagc agacacacct gttggaaatg atcaactgct ggaaatactt 300
aataaattaa tcaaatatcat ccaaattaag tttgttcgtg gtagcacctt caaagaaatc 360
cccgtgactg tctatnagcc aattattaaa aaatacacca aaatcattga tgggagtgcc 420
tgtgggaaat aactgaaaaa gagaccgaga agaacgaatc attacaggtc ctgaaataaaa 480
atacctagga tttctactgg aggtggagaa acagaagaac tctgaagaaa ttgttacaag 540
aagangtccc aaggtcacca aattcattga aggtgggtgat ggtctttatt tgaagatgaa 600
gaaatttaaa gacgcttcag ggagacnccc catgaaggaa ttgccagcca caaaaaaatt 660
cagggattag aaa 673

<210> 33
<211> 673
<212> DNA
<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(673)
 <223> n = A,T,C or G

<400> 33
 actagttatt tacttttcctc cgcttcagaa ggttttttcag actgagagcc taagcatact 60
 ggatctgttg tttctttttg gtctcacctc atcagtgtgc atagtggcag aaattataaa 120
 gaaggttgaa aggagcaggg aaaagatcca gaagcatgtt agttcgacat catcatcttt 180
 tcttgaagta tgatgcatat tgcattattt tatttgcaaa ctaggaattg cagtctgagg 240
 atcatttaga agggcaagtt caagaggata tgaagatttg agaacttttt aactattcat 300
 tgactaaaaa tgaacattaa tgttnaagac ttaagacttt aacctgctgg cagtcccaa 360
 tgaaattatg caactttgat atcatattcc ttgattttaa ttgggctttt gtgattgant 420
 gaaactttat aaagcatatg gtcagttatt tnattaaaaa ggcaaaacct gaaccacctt 480
 ctgcacttaa agaagtctaa cagtacaaat acctatctat cttagatgga tntatttntt 540
 tntattttta aatattgtac tatttatggg nggtggggct ttcttactaa tacacaaatn 600
 aatttatcat ttcaanggca ttctatttgg gtttagaagt tgattccaag nantgcatat 660
 ttcgctactg tnt 673

<210> 34
 <211> 684
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(684)
 <223> n = A,T,C or G

<400> 34
 actagtttat tcaagaaaag aacttactga ttcctctgtt cctaaagcaa gagtggcagg 60
 tgatcagggc tgggtgtagca tccggttcct ttagtgagc taactgcatt tgctactgat 120
 gaccaaggag gaaatcacta agacatttga gaagcagtg tatgaacgtt cttggacaag 180
 ccacagttct gagccttaac cctgtagttt gcacacaaga acgagctcca cctccccctc 240
 ttcaggagga atctgtgcgg atagattggc tggacttttc aatggttctg gtttgcaagt 300
 gggcactgtt atggctgggt atggagcgga cagccccagg aatcagagcc tcagcccggc 360
 tgcctgggtg gaaggtacag gtgttcagca ccttcggaaa aagggcataa agtngtgggg 420
 gacaattctc agtccaagaa gaatgcattg accattgctg gctatttgct tncctagtan 480
 gaattggatn catttttgac cangatnntt ctncatgct ttnttgcaat gaaatcaaat 540
 cccgcattat ctacaagtgg tatgaagtcc tgcnncccc agagaggctg ttcaggcnat 600
 gtcttccaag ggcagggtgg gttacacat tttacctccc ctctcccccc agattatgna 660
 cncagaagga atttntttcc tccc 684

<210> 35
 <211> 614
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(614)
 <223> n = A,T,C or G

<400> 35
 actagtccaa cgcgttngcn aatattcccc tggtagccta cttccttacc cccgaatatt 60

```

ggtaagatcg agcaatggct tcaggacatg gggtctcttc tcctgtgatc attcaagtgc      120
tcaactgcatg aagactggct tgtctcagtg tntcaacctc accagggctg tctcttggtc      180
cacacctcgc tccctgttag tgccgtatga cagcccccat canatgacct tggccaagtc      240
acggtttctc tgtggccaat gttggtnngc tgattgggtg aaagtanggt ggaccaaagg      300
aagncncgtg agcagncanc nccagttctg caccagcagc gcctccgtcc tactnngggg      360
ttcngtttct tcctggccct gngtgggcta nggcctgatt cggggaanatg cctttgcang      420
gaagggganga taantgggat ctaccaattg attctggcaa aacnatntct aagattnttn      480
tgctttatgt ggganacana tctanctctc atttnttget gnanatnaca ccctactcgt      540
gntcgancnc gtcttcgatt ttogganaca cnccantnaa tactggcggt ctgttggttaa      600
aaaaaaaaaa aaaa                                         614

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```

<210> 36
<211> 686
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(686)
<223> n = A,T,C or G

```

```

<400> 36
gtggctggcc cggttctccg cttctcccca tccctactt tcctccctcc ctccctttcc      60
ctccctcgtc gactgttgct tgetggctgc agactccctg acccctccct caccctcccc      120
taacctcggt gccaccgat tgcccttctt ttctgttgct ccagcccagc cctagtgtca      180
gggcgggggc ctggagcagc ccgaggcact gcagcagaag ananaaaaga cacgacnaac      240
ctcagctcgc cagtccggtc gctngcttcc cgccgcatgg caatnagaca gacgcgcgtc      300
acctgctctg ggcacacgcg acccgtaggt gatttggcct tcagtggcat cacccttatg      360
ggtatttctt aatcagcgtc tgcaaagatg gttaacctat gctacgccag ggagatacag      420
gagactggat tggaacattt ttgggggtcta aaggctctgt tgggggtgcaa cactgaataa      480
ggatgccacc aaagcagcta cagcagctgc agatttcaca gcccagtggt gggatgctgt      540
ctcagganat naattgataa cctggctcat aacacattgt caagaatgtg gatttcccca      600
ggatattatt atttgtttac cggggganag gataactgtt tcnctattt taattgaaca      660
aactnaaaca aaanctaagg aaatcc                                         686

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```

<210> 37
<211> 681
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(681)
<223> n = A,T,C or G

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<400> 37
gagacanan nnaacgtcang agaanaaaag angcatggaa cacaanccag gncgatggc      60
caccttccca ccagcancca gcgcccccca gngccccca ngncggang accangactc      120
cancctgnat caatctganc tctattctct gcccattncct acctcgagg tggangccgn      180
aaaggtcgca cmnncagaga agctgctgcc ancaccancc gccccnnccc tgnccgggctn      240
nataggaaac tggtagccnn gctgcanaat tcatacagga gcacgcgang ggacnncnct      300
cacactgagt tnnngatgan gctnaccan ggacctnccc cagcnnattg annacnggac      360
tgccggaggaa ggaagacccc gnacnggatc ctggccggcn tgccaccccc ccacccttag      420
gattatnccc cttgactgag tctctgaggg gctacccgaa cccgcctcca ttccctacca      480
natnntgctc natcgggact gacangctgg ggatnggagg ggctatcccc cancatcccc      540

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tnanaccaac agcnacngan natnggggct cccnngggte gnggcaacnc tectncaccc 600
cgggcgnggc cttegggtnt gtectcctc aacnaattcc naaanggcgg gcccccngt 660
ggactcctcn ttgttcctc c 681

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<210> 38
<211> 687
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(687)
<223> n = A,T,C or G

```

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<400> 38
canaaaaaaa aaaacatggc cgaaaccagn aagctgcgcg atggcgccac ggccccctctt 60
ctcccgccct gtgtccggaa ggtttcctc cgaggcgccc cggctccgc aagcggagga 120
gagggcgagg cntgcgggg cgagagctca naggccctgg ggcgctctg ctctcccgcc 180
atcgcaaggg cggcgctaac ctnaggctc cccgcaaagg tcccnange gngggcgggc 240
gggggctgtg anaaccgcaa aaanaacgct gggcgcgeng cgaaccgctc ccccccgcg 300
aaggananac ttccacagan gcagcgtttc cacagccan agccacnttt ctaggggtgat 360
gcaccccgat aagttcctgn cggggaagct caccgctgtc aaaaaanctc ttegtccac 420
cggcgcacna agggggangan ggcangangc tgccgcccgc acaggtcatc tgatcacgtc 480
gcccgcctta ntctgctttt gtgaatctcc actttgttca accccacccg cegtctctc 540
ctccttgcgc ctctctctna ccttaanaac cagcttctc taccnatng tanttntctc 600
gcnenngtng aaattaattc ggtecnccgg aacctcttnc ctgtggcaac tgctnaaaga 660
aactgctgtt ctgnntactg cngtccc 687

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<210> 39
<211> 695
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(695)
<223> n = A,T,C or G

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```

<400> 39
actagtctgg cctacaatag tgtgattcat gtaggacttc tttcatcaat tcaaaacccc 60
tagaaaaacg tatacagatt atataagtag ggataagatt tctaacattt ctgggctctc 120
tgacccctgc gctagactgt ggaaaggagg tattattata gtatacaaca ctgctgttgc 180
cttattagtt ataacatgat aggtgctgaa ttgtgattca caatttaaaa acactgtaat 240
ccaaactttt ttttttaact gtagatcatg catgtgaatg ttaatgttaa tttgttcaan 300
gttggttatgg gtagaaaaaa ccacatgcct taaaatttta aaaagcaggg cccaaactta 360
ttagtttaaa attaggggta tgtttccagt ttgttattaa ntgggttatag ctctgttttag 420
aanaaatcna ngaacangat ttngaaantt aagntgacat tatttnccag tgacttgta 480
atttgaaatc anacacggca ccttcggtt ttgttctatt ggnntttgaa tccaancngg 540
ntccaaatct tnttggaac ngtcnnttta acttttttac nanatcttat ttttttatt 600
tggaatggcc ctatttaang ttaaaagggg ggggnnccac naccattcnt gaataaaact 660
naatatatat ccttggtccc ccaaaattta agng 695

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<210> 40
<211> 674
<212> DNA

```


<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (674)

<223> n = A,T,C or G

<400> 40

actagtagtc	agttgggagt	ggttgctata	ccttgacttc	atztatatga	atttccactt	60
tattaaataa	tagaaaagaa	aatcccgggtg	cttgccagtag	agttatagga	cattctatgc	120
ttacagaaaa	tatagccatg	attgaaatca	aatagtaaag	gctgttctgg	ctttttatct	180
tcttagctca	tcttaaataa	gtagtacact	tgggatgcag	tgcgtctgaa	gtgctaataca	240
gttgtaacaa	tagcacaaat	cgaacttagg	atgtgtttct	tctcttctgt	gtttcgattt	300
tgatcaatte	tttaattttg	ggaacctata	atacagtttt	cctattcttg	gagataaaaa	360
ttaaattggat	cactgatatt	taagtcattc	tgcttctcat	ctnaatattc	catattctgt	420
attagganaa	antacctccc	agcacagccc	cctctcaaac	cccacccaaa	accaagcatt	480
tggaatgagt	ctccttttatt	tccgaantgt	ggatggtata	acccatatacn	ctccaatttc	540
tgnttgggtt	gggtattaat	ttgaactgtg	catgaaaagn	ggnaatcttt	nctttgggtc	600
aaantttnc	ggttaatttg	nctngncaaa	tccaatttnc	tttaagggtg	tctttataaa	660
atttgctatt	cngg					674

<210> 41

<211> 657

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (657)

<223> n = A,T,C or G

<400> 41

gaaacatgca	agtaccacac	actgtttgaa	ttttgcacaa	aaagtgactg	tagggatcag	60
gtgatagccc	cggaaatgtac	agtgtcttgg	tgcaccaaga	tgccttctaa	aggctgacat	120
accttgggac	cctaattgggg	cagagagtat	agccctagcc	cagtgggtgac	atgaccactc	180
cctttggggag	gctgaagtta	aaggggaatgg	tatgtgtttt	ctcatggaag	cagcacatga	240
atnggtnaca	ngatgttaaa	ntaaggntct	antttgggtg	tcttgtcatt	tgaaaaantg	300
acacactcct	ancanctggg	aaaggggtgc	tggaaagccat	ggaagaactc	taaaaacatt	360
agcatgggct	gatctgatta	cttcctggca	tcccgtcac	ttttatggga	agtcttatta	420
naaggatggg	ananttttcc	atatacttgc	tgttggaact	ctggaacact	ctctaaattt	480
ccctctatta	aaaatcactg	nccttactac	acttctctct	tganggaata	gaaatggacc	540
tttctctgac	ttagttcttg	gcatggganc	cagcccaaat	taaaatctga	cttntccggt	600
ttctcngaa	ctcacctact	tgaattggta	aaacctcctt	tgggaattagn	aaaaacc	657

<210> 42

<211> 389

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (389)

<223> n = A,T,C or G

<400> 42

actagtgtctg	aggaatgtaa	acaagtttgc	tgggccttgc	gagacttcac	caggttgttt	60
cgatagctca	cactcctgca	ctgtgcctgt	caccagga	tgtctttttt	aattagaaga	120
caggaagaaa	acaaaaacca	gactgtgtcc	cacaatcaga	aacctccgtt	gtggcagang	180
ggccttcacc	gccaccaggg	tgtcccgcca	gacagggaga	gactccagcc	ttctgaggcc	240
atcctgaaga	attcctgttt	gggggttgtg	aagggaaatc	acccggattt	aaaaagatgc	300
tgttgctgc	ccgcgtngtn	gggaagggac	tggtttctctg	gtgaatttct	taaaagaaaa	360
atattttaag	ttaagaaaaa	aaaaaaaaa				389

<210> 43

<211> 279

<212> DNA

<213> Homo sapien

<400> 43

actagtgtgaca	agctcctggg	cttgagatgt	cttctcggtta	aggagatggg	ccttttggag	60
gtaaaggata	aatgaatga	gttctgtcat	gattcactat	tctagaactt	gcatgacctt	120
tactgtgtta	gctctttgaa	tgttcttgaa	attttagact	ttctttgtaa	acaaataata	180
tgtccttatc	attgtataaa	agctgttatg	tgcaacagtg	tggagatcct	tgtctgattt	240
aataaaatac	ttaaactactg	aaaaaaaaa	aaaaaaaaa			279

<210> 44

<211> 449

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(449)

<223> n = A,T,C or G

<400> 44

actagtagca	tcttttctac	aacgttaaaa	ttgcagaagt	agcttatcat	taaaaaacia	60
caacaacaac	aataacaata	aatcctaagt	gtaaatcagt	tattctaccc	cctaccaagg	120
atatcagcct	gttttttccc	ttttttctcc	tgggaataat	tgtgggcttc	ttcccaaatt	180
tctacagcct	ctttcctctt	ctcatgcttg	agcttccttg	tttgcacgca	tgcgttgtgc	240
aagantgggc	tgtttngctt	ggantncggg	ccnagtggaa	ncatgctttc	ccttgttact	300
gttgaagaa	actcaaacct	tcnancctta	ggtgttncca	ttttgtcaag	tcatcactgt	360
atttttgtac	tggcattaac	aaaaaaaaagaa	atnaaatatt	gttccattaa	actttaataa	420
aactttaaaa	gggaaaaaaa	aaaaaaaaa				449

<210> 45

<211> 559

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(559)

<223> n = A,T,C or G

<400> 45

actagtgtgg	gggaatcacg	gacacttaaa	gtcaatctgc	gaaataattc	ttttattaca	60
cactcactga	agtttttgag	tcccagagag	ccattctatg	tcaaacattc	caagtactct	120
ttgagagccc	agcattacat	caacatgccc	gtgcagttca	aaccgaagtc	cgcaggcaaa	180
tttgaagctt	tgcttgtcat	tcaaacagat	gaaggcaaga	gtattgctat	tcgactaatt	240

ggtgaagctc	ttggaaaaaa	ttnactagaa	tactttttgt	gttaagttaa	ttacataagt	300
tgtattttgt	taactttatc	tttctacact	acaattatgc	ttttgtatat	atattttgta	360
tgatggatat	ctataattgt	agattttgtt	tttacaagct	aatactgaag	actcgactga	420
aatattatgt	atctagccca	tagtattgta	cttaactttt	acagggtgaa	aaaaaaattc	480
tgtgtttgca	ttgattatga	tattctgaat	aaatatggga	atatatttta	atgtgggtaa	540
aaaaaaaaaa	aaaaaggaa					559

<210> 46

<211> 731

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(731)

<223> n = A,T,C or G

<400> 46

actagttcta	gtaccatggc	tgatcatagat	gcaaccatta	tattccattt	agtttcttcc	60
tcaggttccc	taacaattgt	ttgaaactga	atatatatgt	ttatgtatgt	gtgtgtgttc	120
actgtcatgt	atatgggtga	tatgggatgt	gtgcagtttt	cagttatata	tatattcata	180
tatacatatg	catatatatg	tataatatac	atatatacat	gcatacactt	gtataatata	240
catatatata	cacatatatg	cacacatatn	atcactgagt	tccaaagtga	gtctttattt	300
ggggcaattg	tattctctcc	ctctgtctgc	tcactgggcc	tttgcaagac	atagcaattg	360
cttgatttcc	tttgataaag	agtccttctc	tcggcactct	tgactctagc	cttaacttta	420
gatttctatt	ccagaatacc	tctcatatct	atcttaaaac	ctaaganggg	taaagangtc	480
ataagattgt	agtatgaaag	antttgctta	gttaaattat	atctcaggaa	actcattcat	540
ctacaaatta	aattgtaaaa	tgatggtttg	ttgtatctga	aaaaatgttt	agaacaagaa	600
atgtaactgg	gtacctgtta	tatcaaagaa	cctcnattta	ttaagtctcc	tcatagccan	660
atccttatat	ngccctctct	gacctgantt	aatananact	tgaataatga	atagtttaatt	720
taggnntggg	c					731

<210> 47

<211> 640

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(640)

<223> n = A,T,C or G

<400> 47

tgcgngccgg	tttggccctt	ctttgtanga	cactttcattc	cgccctgaaa	tcttcccgat	60
cgtaataaac	tcctcaggtc	cctgcctgca	caggggtttt	tcttantttg	ttgcctaaca	120
gtacaccaaa	tgtgacatcc	tttcaccaat	atngattnct	tcataccaca	tcntcnatgg	180
anacgactnc	aacaattttt	tgatnaccen	aaanactggg	ggctnnaana	agtacantct	240
ggagcagcat	ggacctgtcn	gcnactaang	gaacaanagt	nntgaacatt	tacacaacct	300
ttggtatgtc	ttactgaaag	anagaaacat	gcttctnncc	ctagaccacg	aggncaaccg	360
caganattgc	caatgccaaag	tccgagcggg	tagatcagggt	aatacattcc	atggatgcat	420
tacatacntt	gtccccgaaa	nanaagatgc	cctaanggct	tcttcanact	ggccngaaa	480
acantacac	ctgggtgcttg	ganaacanac	tctttggaag	atcatctggc	acaagttccc	540
cccagtgggg	tttnccttgg	cacctanctt	accanatcna	ttcggaancc	attctttggc	600
ntggcnttnt	nttgggacca	ntcttctcac	aactgnaccc			640

<210> 48
 <211> 257
 <212> DNA
 <213> Homo sapien

<400> 48
 actagtatat gaaaatgtaa atatcacttg tgtactcaaa caaaagttgg tcttaagctt 60
 ccaccttgag cagccttgga aacctaacct gcctctttta gcataatcac attttctaaa 120
 tgattttctt tgttcctgaa aaagtgattt gtattagttt tacatttggt ttttggaaga 180
 ttatatttgt atatgtatca tcataaaaata tttaaataaa aagtatcttt agagtgaaaa 240
 aaaaaaaaaa aaaaaaa 257

<210> 49
 <211> 652
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (652)
 <223> n = A,T,C or G

<400> 49
 actagttcag atgagtggct gctgaagggg ccccttgctc attttcatta taacccaatt 60
 tccacttatt tgaactctta agtcataaat gtataatgac ttatgaatta gcacagttaa 120
 gttgacacta gaaactgccc atttctgtat tacactatca aataggaaac attggaaaga 180
 tggggaaaaa aatcttattt taaaatggct tagaaagttt tcagattact ttgaaaattc 240
 taaacttctt tctgtttcca aaacttgaaa atatgtagat ggactcatgc attaagactg 300
 ttttcaaaagc tttcctcaca tttttaaagt gtgattttcc ttttaatatata catatttatt 360
 ttcttttaaag cagctatata ccaacccatg actttggaga tatacctatn aaaccaatat 420
 aacagcangg ttattgaagc agctttctca aatgttgctt cagatgtgca agttgcaa 480
 tttattgtat ttgtanaata caatttttgt tttaaactgt atttcaatct atttctccaa 540
 gatgcttttc atatagagtg aaatatccca ngataactgc ttctgtgtcg tcgcatttga 600
 cgcataactg cacaaatgaa cagtgtatata ctcttggttg tgcattnacc cc 652

<210> 50
 <211> 650
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (650)
 <223> n = A,T,C or G

<400> 50
 ttgcgctttg attttttttag ggcttgtgcc ctgtttcact tataggggtct agaatgcttg 60
 tgttgagtaa aaaggagatg cccaatatc aaagctgcta aatgttctct ttgccataaa 120
 gactccgtgt aactgtgtga acacttgga tttttctcct ctgtcccagag gtcgtcgtct 180
 gctttctttt ttgggttctt tctagaagat tgagaaatgc atatgacagg ctgagancac 240
 ctccccaaac acacaagctc tcagccacan gcagcttctc cacagcccca gcttcgcaca 300
 ggctcctgga nggctgcctg ggggaggcag acatgggagt gccaaagggtg ccagatgggt 360
 ccaggactac aatgtcttta tttttaactg tttgccactg ctgccctcac ccctgcccgg 420
 ctctggagta ccgtctgccc canacaagtg ggantgaaat ggggggtggg gggaaactg 480
 attcccantt agggggtgcc taactgaaca gtagggatan aagggtgtgaa cctgngaant 540

gctttttataa atttatnttcc ttgttanatt tatttttttaa tttaatctct gttnaactgc 600
ccngggaaaaa ggggaaaaaa aaaaaaaaat tctnttttaa cacatgaaca 650

<210> 51
<211> 545
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(545)
<223> n = A,T,C or G

<400> 51
tggcgtgcaa ccagggtagc tgaagtttgg gtctgggact ggagattggc cattaggcct 60
cctganattc cagctccctt ccaccaagcc cagtcttgct acgtggcaca gggcaaacct 120
gaactccctt gggcctcagt tccccctccc ctccatgana tgaaaagaat actacttttt 180
cttgttggtc taacnttgct ggacncaaag tgtngtcatt attggtgtat tgggtgatgt 240
gtncaaaact gcagaagctc actgcctatg agaggaanta agagagatag tggatganag 300
ggacanaagg agtcattatt tggatatagat ccacccttcc caacctttct ctccctcagtc 360
cctgcncctc atgtntctgg tntggtgagt cctttgtgcc accanccatc atgctttgca 420
ttgctgccat cctgggaagg gggtnatcg tctcacaact tggtgtcatc gtttganatg 480
catgctttct tnatnaaaca aanaaannaa tgtttgacag ngtttaaaat aaaaaanaaa 540
caaaa 545

<210> 52
<211> 678
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(678)
<223> n = A,T,C or G

<400> 52
actagtagaa gaactttgcc gcttttgtgc ctctcacagg cgcctaaagt cattgccatg 60
ggaggaagac gatttggggg gggagggggg gggggcangg tccgtggggc ttteccctant 120
ntatctccat ntccantggn cnntgtcgcc tcttccctcg tencattnga anttantccc 180
tggneccenn nccctctccn nctnncct cccctcccg nncctccnn cttttntan 240
ncttccccat ctccntcccc cctnanngtc ccaacnccgn cagcaatnnc ncaettntctc 300
nctcncncc tccnccggtt cttctnttct enacntntnc ncnntnccn tgccnntnaa 360
annctctccc cnetgcaanc gattctctcc ctcenennan ctntccactc cntncttctc 420
nncgctect nttentcnc ccacctctc ccttcgnccc cantacnctc ncnccecttn 480
cgnntenttn nnntcctcnn accnccncc tcccttncnc cctcttctcc cgggtntntc 540
tctctccnc nncnncncc cncnccctc nngcgnccnt tccgccccn cncnccntt 600
ccttctcnc cantccatcn cntntnccat nctnccncc nctcncncc gctnccccn 660
ntctcttca cacngtcc 678

<210> 53
<211> 502
<212> DNA
<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(502)

<223> n = A,T,C or G

<400> 53

tgaagatcct	ggtgtcgcca	tggggccgccg	ccccgcccggt	tgttaccgggt	attgtaagaa	60
caagccgtac	ccaaagtctc	gcttctgccg	aggtgtccct	gatgccaaaa	ttcgattttt	120
tgacctgggg	cggaaaaang	caaaantgga	tgagtctccg	ctttgtggcc	acatgggtgtc	180
agatcaatat	gagcagctgt	cctctgaagc	cctgnangct	gcccgaattt	gtgccaataa	240
gtacatggta	aaaagtngtg	gcnaagatgc	ttccatatcc	gggtgcggn	ccaccccttc	300
cacgtcatcc	gcatacaaa	gatgttggtc	tgtgctgggg	ctgacaggct	cccaacaggc	360
atgcgaagtg	cctttggaaa	acccanggca	ctgtggccag	ggttcacatt	gggccaattn	420
atcatgttca	tccgcaccaa	ctgcagaaca	angaacntgt	naattnaagc	cctgcccagg	480
gncaanttca	aatttcccg	cc				502

<210> 54

<211> 494

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(494)

<223> n = A,T,C or G

<400> 54

actagtccaa	gaaaaatatg	cttaatgtat	attacaaagg	ctttgtatat	gttaacctgt	60
tttaatgcca	aaagtttgtc	ttgtccacaa	tttccttaag	acctcttcag	aaagggattt	120
gtttgcctta	atgaatactg	ttgggaaaaa	acacagtata	atgagtgaaa	agggcagaag	180
caagaaattt	ctacatctta	gagactccaa	gaagaatgag	tatccacatt	tagatggcac	240
attatgagga	ctttaatctt	tccttaaaca	caataatgtt	ttcttttttc	ttttattcac	300
atgatttcta	agtatatctt	tcatgcagga	cagtttttca	accttgatgt	acagtgactg	360
tggttaaattt	ttctttcagt	ggcaacctct	ataatcttta	aaatatgggtg	agcatcttgt	420
ctgtttttgaa	ngggatatga	cnatnaatct	atcagatggg	aaatcctgtt	tccaagttag	480
aaaaaaaaaa	aaaa					494

<210> 55

<211> 606

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(606)

<223> n = A,T,C or G

<400> 55

actagtaaaa	agcagcattg	ccaaataatc	cctaattttc	cactaaaaat	ataatgaaat	60
gatgttaagc	tttttgaaaa	gtttagggtta	aacctactgt	tgtagatta	atgtatttgt	120
tgcttccctt	tatctggaat	gtggcattag	cttttttatt	ttaaccctct	ttaattctta	180
ttcaattcca	tgacttaagg	ttggagagct	aaacactggg	atttttggat	aacagactga	240
cagttttgca	taattataat	cggcattgta	catagaaagg	atatggctac	cttttggttaa	300
atctgcactt	tctaaatata	aaaaaaggga	aatgaagtat	aaatcaattt	ttgtataatc	360
tgtttgaaac	atgantttta	tttgcttaat	attanggctt	tgcccttttc	tgtagtctc	420
ttgggatcct	gtgtaaaact	gttctcatta	aacaccaaac	agttaagtec	attctctggt	480

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actagctaca aattccgttt catattctac ntaacaatth aaattaactg aaatatttct 540
anatggtcta cttctgtcnt ataaaaacna aacttgantt nccaaaaaaa aaaaaaaaaa 600
aaaaaa 606

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<210> 56
<211> 183
<212> DNA
<213> Homo sapien

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<400> 56
actagtatat ttaaacttac aggcttattt gtaatgtaaa ccaccatttt aatgtactgt 60
aattaacatg gttataatac gtacaatcct tccctcatcc catcacacaa ctttttttgt 120
gtgtgataaa ctgatttttg tttgcaataa aaccttgaaa aataaaaaaa aaaaaaaaaa 180
aaa 183

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<210> 57
<211> 622
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(622)
<223> n = A,T,C or G

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<400> 57
actagtcact actgtcttct ccttgtagct aatcaatcaa tattcttccc ttgcctgtgg 60
gcagtggaga gtgctgctgg gtgtacgctg cacctgccca ctgagttggg gaaagaggat 120
aatcagtgag cactgttctg ctgagagctc ctgatctacc ccaccccta ggatccagga 180
ctgggtcaaa gctgcatgaa accaggccct ggcagcaacc tgggaatggc tggaggtggg 240
agagaacctg acttctcttt cctctccct cctccaacat tactggaact ctatcctgtt 300
agggatcttc tgagcttggt tccctgctgg gtgggacaga agacaaagga gaagggangg 360
tctacaanaa gcagcccttc tttgtcctct ggggttaatg agcttgacct ananttcag 420
gaganaccan aagcctctga tttttaattt ccntnaaatg tttgaagtnt atatntacat 480
atatatattt ctttnaatnt ttgagtcttt gatatgtctt aaaatccant ccctctgccn 540
gaaacctgaa ttaaaacct gaanaaaat gtttncctta aagatgttan taattaattg 600
aaacttgaaa aaaaaaaaaa aa 622

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<210> 58
<211> 433
<212> DNA
<213> Homo sapien

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<400> 58
gaacaaattc tgattgggta tgtaccgtca aaagacttga agaaatttca tgattttgca 60
gtgtggaagc gttgaaaatt gaaagtact gcttttccac ttgctcatat agtaaagga 120
tcctttcagc tgccagtgtt gaataatgta tcatccagag tgatgttatc tgtgacagtc 180
accagcttta agctgaacca ttttatgaat accaaataaa tagacctctt gtactgaaaa 240
catatttggt actttaatcg tgctgcttgg atagaaatat ttttactggt tcttctgaat 300
tgacagtaaa cctgtccatt atgaatggcc tactgttcta ttatttggtt tgacttgaat 360
ttatccacca aagacttcat ttgtgtatca tcaataaagt tgtatgtttc aactgaaaaa 420
aaaaaaaaa aaa 433

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<210> 59
<211> 649

```

<212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(649)
 <223> n = A,T,C or G

<400> 59
 actagttatt atctgacttt cnggttataa tcattctaata gagtgtgaag tagcctctgg 60
 tgtcatttgg atttgcattt ctctgatgag tgatgctatc aagcaccttt gctgggtgctg 120
 ttggccatat gtgtatgttc cctggagaag tgtctgtgct gagccttggc ccacttttta 180
 attaggcgtn tgtcttttta ttactgagtt gtaaganttc tttatatatt ctggattcta 240
 gacccttatac agatacatgg tttgcaaata tttctctcca ttctgtgggt tgtgttttca 300
 ctttatcgat aatgtcctta gacatataat aaatttgtat tttaaaagtg acttgatttg 360
 ggctgtgcaa ggtgggctca cgcttgtaat ccagcactt tgggagactg aggtgggtgg 420
 atcatatgan gangctagga gttcgaggtc agcctggcca gcatagcgaa aacttgtctc 480
 tacnaaaaaat acaaaaatta gtcaggcatg gtgggtgcacg tctgtaatac cagcttctca 540
 ggangctgan gcacaaggat cacttgaacc ccagaangaa gangttgcag tganctgaag 600
 atcatgccag ggcaacaaaa atgagaactt gtttaaaaaa aaaaaaaaaa 649

<210> 60
 <211> 423
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(423)
 <223> n = A,T,C or G

<400> 60
 actagttcag gccttccagt tcaactgacaa acatggggaa gtgtgcccag ctggctggaa 60
 acctggcagt gataccatca agcctgatgt ccaaaagagc aaagaatatt tctccaagca 120
 gaagtgagcg ctgggctgtt ttagtgccag gctgcggtgg gcagccatga gaacaaaacc 180
 tcttctgtat ttttttttcc cattagтана acacaagact cngattcagc cgaattgtgg 240
 tgtcttacaa ggcagggctt tctacaggg ggtgganaaa acagcctttc ttccttgggt 300
 aggaatggcc tgagttggcg ttgtgggcag gctactgggt tgtatgatgt attagtagag 360
 caaccatta atcttttgta gtttgatatna aactganct gagacctta aaaaaaaaaa 420
 aaa 423

<210> 61
 <211> 423
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(423)
 <223> n = A,T,C or G

<400> 61
 cgggactgga atgtaaagtg aagttcggag ctctgagcac gggctcttcc cgccgggtcc 60
 tccctcccca gacccagag ggagaggccc accccgcccc gcccgcccc agccctgct 120
 caggtctgag tatggctggg agtcgggggc cacaggcctc tagctgtgct gctcaagaag 180

actggatcag	ggtanctaca	agtggccggg	ccttgccttt	gggattctac	cctgttccta	240
atttggtgtt	ggggtgcggg	gtccctggcc	cccttttcca	cactncctcc	ctccngacag	300
caacctccct	tggggcaatt	gggcctggnt	ctccncccg	tgttgcnacc	ctttgttggt	360
ttaaggncct	taaaaatgtt	annttttccc	ntgccnggg	taaaaaagga	aaaaactnaa	420
aaa						423

<210> 62
 <211> 683
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(683)
 <223> n = A,T,C or G

<400> 62						
gctggagagg	ggtacggact	ttcttggagt	tgtcccaggt	tggaatgaga	ctgaactcaa	60
gaagagaccc	taagagactg	gggaatgggt	cctgccttca	ggaaagtga	agacgcttag	120
gctgtcaaca	cttaaaaggaa	gtcccttga	agccagagt	ggacagacta	gacccattga	180
tggggccact	ggccatggtc	cgtggacaag	acattccngt	gggccatggc	acaccggggg	240
ggatcaaaat	gtgtacttgt	ggggtctcgc	cccttgccaa	aaccaaacca	ntcccactcc	300
tgtcnttga	ctttcttccc	attccctcct	ccccaaatgc	acttcccctc	ctccctctgc	360
ccctcctgtg	tttttggaa	tctgtttccc	tcaaaaattgt	taatttttta	nttttngacc	420
atgaacttat	gtttggggtc	nangttcccc	ttnccaatgc	ataactaatat	attaatgggt	480
atttattttt	gaaatatttt	ttaatgaact	tggaaaaaat	tnntggaatt	tccttncttc	540
cntttntttt	gggggggggtg	gggggntggg	ttaaaaatttt	tttggaancc	cnatnggaaa	600
ttnttacttg	gggccccct	naaaaaantn	anttccaatt	cttnnatngc	ccctnttccn	660
ctaaaaaaaa	ananannaaa	aan				683

<210> 63
 <211> 731
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(731)
 <223> n = A,T,C or G

<400> 63						
actagtcata	aaggggtgtg	gcgtcttcga	cgtggcggtc	ttggcgccac	tgctgcgaga	60
cccggccctg	gacctcaagg	tcatccaatt	ggtgcgtgat	ccccgcgcgg	tggcgagttc	120
acggatccgc	tcgcgccacg	gcctcatccg	tgagagccta	caggtgggtg	gcagccgaga	180
ccgcgagctc	accgcatgcc	cttcttggag	gccgcggggc	acaagcttgg	cgcccanaaa	240
gaaggcgtn	ggggcccgc	aantaccacg	ctctgggcgc	tatggaangt	cctcttgcaa	300
taatattggt	tnaaaanctg	canaanagcc	cctgcanccc	cctgaactgg	gntgcagggc	360
cncttacctn	gtttggntgc	ggttacaaa	aacctgtttn	ggaaaaccct	nccnaaaacc	420
ttccgggaaa	attntncaaa	ttttnttgg	ggaattnttg	ggtaaaccct	ccnaaaatgg	480
gaaaacnttt	tgccctnnaa	antaaaccat	tnggttccgg	ggggcccccc	ncaaaaccct	540
ttttnttttt	ttntgcccc	cantnncccc	ccggggcccc	tttttttngg	ggaaaaancc	600
ccccctncc	nanantttta	aaagggnngg	anaatttttn	nttncccccc	gggncccccn	660
ggngntaaaa	nggtttcncc	cccccgagg	gnggggnnnc	ctcnnaaacc	cntntcnna	720
ccncttttn	n					731

<210> 64
 <211> 313
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)... (313)
 <223> n = A,T,C or G

<400> 64
 actagttgtg caaaccacga ctgaagaaag acgaaaagtg ggaaataact tgcaacgtct 60
 gttagagatg gttgctacac atgttgggtc tgtagagaaa catcttgagg agcagattgc 120
 taaagttgat agagaatatg aagaatgcat gtcagaagat ctctcggaaa atattaaaga 180
 gattagagat aagtatgaga agaaagctac tctaattaag tcttctgaag aatgaagatn 240
 aaatgttgat catgtatata tatccatagt gaataaaatt gtctcagtaa agttgtaaaa 300
 aaaaaaaaaa aaa 313

<210> 65
 <211> 420
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)... (420)
 <223> n = A,T,C or G

<400> 65
 actagttccc tggcaggcaa gggcttccaa ctgaggcagt gcatgtgtgg cagagagagg 60
 caggaagctg gcagtggcag cttctgtgtc tagggagggg tgtggctccc tccctccctg 120
 tctgggaggt tggagggaag aatctaggcc ttagcttgcc ctccctgccac ccttcccctt 180
 gtagatactg ccttaacact ccttcctctc tcagctgtgg ctgccacca agccaggttt 240
 ctccgtgctc actaatttat ttccaggaaa ggtgtgtgga agacatgagc cgtgtataat 300
 atttgtttta acattttcat tgcaagtatt gaccatcatc cttggtgtgt tatcgttgta 360
 acacaaatta atgatattaa aaagcatcca aacaaagccn annnnnaana nnannngaaa 420

<210> 66
 <211> 676
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)... (676)
 <223> n = A,T,C or G

<400> 66
 actagtttcc tatgatcatt aaactcattc tcagggttaa gaaaggaatg taaatttctg 60
 cctcaatttg tacttcatca ataagttttt gaagagtgcg gatttttagt caggctcttaa 120
 aaataaactc acaaatctgg atgcatttct aaattctgca aatgtttcct ggggtgactt 180
 aacaaggaat aatcccacaa tatacctagc tacctaatac atggagctgg ggctcaaccc 240
 actgttttta aggatttgcg cttacttgtg gctgaggaaa aataagtagt tccgagggaa 300
 gtagttttta aatgtgagct tatagatngg aaacagaata tcaacttaat tatggaaatt 360
 gttagaaacc tgttctcttg ttatctgaat cttgattgca attactattg tactggatag 420

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actccagccc attgcaaagt ctcagatatc ttanctgtgt agttgaattc cttggaaatt      480
ctttttaaga aaaaattgga gtttnaaaga aataaacccc tttgttaaatt gaagcttggc      540
tttttggtga aaaanaatca tcccgcaggg cttattgttt aaaaanggaa ttttaagcct      600
ccctggaaaa anttgttaat taaatgggga aaatgntggg naaaaattat ccgttagggt      660
ttaaagggaa aactta                                     676

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<210> 67
<211> 620
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(620)
<223> n = A,T,C or G

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<400> 67
caccattaaa gctgcttacc aagaacttcc ccagcatttt gacttccttg tttgatagct      60
gaattgtgag caggtgatag aagagccttt ctagttgaac atacagataa tttgctgaat      120
acattccatt taatgaaggg gttacatctg ttacgaagct actaagaagg agcaagagca      180
taggggaaaa aaatctgac agaacgcac aaactcacat gtgccccctc tactacaaac      240
agattgtagt gctgtggtgg tttattccgt tgtgcagaac ttgcaagctg agtcactaaa      300
cccaaagaga ggaaattata ggttagttaa acattgtaat ccaggaact aagtttaatt      360
cacttttgaa gtgttttggt ttttattttt ggtttgctctg atttactttg ggggaaaang      420
ctaaaaaaaa agggatatca atctctaatt cagtgccccc taaaagtgtg ccctaaaaag      480
tctttactgg aanttatggg actttttaag ctccaggntt tttggtcctc caaattaacc      540
ttgcatgggc cccttaaaat tgttgaangg cattcctgcc tctaagtttg gggaaaattc      600
ccccnttttn aaaatttgga                                     620

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<210> 68
<211> 551
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(551)
<223> n = A,T,C or G

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<400> 68
actagtagct ggtacataat cactgaggag ctatttctta acatgctttt atagaccatg      60
ctaattgctag accagtattt aagggetaat ctcacacctc ctagctgta agagtctggc      120
ttagaacaga cctctctgtg caataacttg tggccactgg aaatecctgg gccggcattt      180
gtattggggg tgcaatgact cccaagggcc aaaagagtta aaggcacgac tgggatttct      240
tctgagactg tggtgaaact ccttccaagg ctgagggggg cagtangtgc tctgggaggg      300
actcggcacc actttgatat tcaacaagcc acttgaagcc caattataaa attgttattt      360
tacagctgat ggaactcaat ttgaaccttc aaaactttgt tagtttatcc tattatattg      420
ttaaacctaa ttacatttgt ctagcattgg atttggttcc tgtngcatat gttttttcn      480
cctatgtgct ccctccccc nmatcttaat ttaaaccnca attttgcnat tcnecnnnnn      540
nannnnanna a                                     551

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<210> 69
<211> 396
<212> DNA
<213> Homo sapien

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<220>
 <221> misc_feature
 <222> (1)...(396)
 <223> n = A,T,C or G

<400> 69
 cagaaatgga aagcagagtt ttcattttctg tttataaaacg tctccaaaca aaaatggaaa 60
 gcagagtttt cattaaatcc ttttaccttt tttttttctt ggtaatcccc tcaaataaca 120
 gtatgtggga tattgaatgt taaagggata tttttttcta ttatttttat aattgtacaa 180
 aattaagcaa atgttaaaaag ttttatatgc tttattaatg ttttcaaaag gtatnatata 240
 tgtgatacat tttttaagct tcagttgctt gtcttctggt actttctggt atgggctttt 300
 ggggagccan aaaccaatct acnatctctt tttgtttgcc aggacatgca ataaaattta 360
 aaaaataaat aaaaactatt nagaaattga aaaaaa 396

<210> 70
 <211> 536
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(536)
 <223> n = A,T,C or G

<400> 70
 actagtgcga aagcaaatat aaacatcgaa aaggcggttcc tcacgtagc tgaagatata 60
 cttcgaaaga cccctgtaaa agagcccaac agtgaaaatg tagatatcag cagtggagga 120
 ggcgtgacag gctggaagag caaatgctgc tgagcattct cctgttccat cagttgccat 180
 ccactacccc gttttctctt cttgctgcaa aataaaccac tctgtccatt ttttaactcta 240
 aacagatatt tttgtttctc atcttaacta tccaagccac ctattttatt tggtctttca 300
 tctgtgactg cttgctgact ttatcataat tttcttcaaa caaaaaaatg tatagaaaaa 360
 tcatgtctgt gacttcattt ttaaatgnta cttgctcagc tcaactgcat ttcagttggt 420
 ttatagtcca gttcttatca acattnaaac ctatngcaat catttcaaat ctattctgca 480
 aattgtataa gaataaaagt tagaatttaa caattaaaaa aaaaaaaaaa aaaaaa 536

<210> 71
 <211> 865
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(865)
 <223> n = A,T,C or G

<400> 71
 gacaaagcgt taggagaaga anagaggcag ggaanactnc ccaggcacga tggccncctt 60
 cccaccagca accagcgccc cccaccagcc cccaggcccc gacgacgaag actccatcct 120
 ggattaatct nacctctntc gcctgnccca ttccctacctc ggaggtggag gccggaaaag 180
 tcncaccaag aganaantc ctgccaacac caaccgcccc agccctggcg ggcacganag 240
 gaaactggcg accaatctgc agaattctna gaggaanaag cnaggggccc cgcgctnaga 300
 cagagctgga tatgangcca gaccatggac nctacnccn ncaatncana cgggactgcg 360
 gaagatggan gaccncgac nngatcagcg cngctnncca nccccccacc cctatgaatt 420
 attccccgctg aangaatctc tgannggctt ccannaaagc gcctccccnc cnaacgnaan 480

tncaacatng	ggattanang	ctgggaactg	naaggggcaa	ancctnnaat	atccccagaa	540
acaanctctc	ccnaanaaac	tggggcncct	catnggtggn	accaactatt	aactaaaccg	600
cacgccaagn	aantataaaa	ggggggcccc	tcnccggng	accccccttt	gtcccttaat	660
ganggttate	cnccttgctg	accatggtnc	ccnnttctgt	ntgnatgttt	ccnctccccct	720
ccncttatnt	cnagccgaac	tcnnatttnc	ccgggggtgc	nacnancng	tnccnctttn	780
ttngttgncc	cngcccttcc	cgnccgaacn	cgtttccccg	ttantaacgg	cacccggggg	840
aagggtgntt	ggccccctcc	ctccc				865

<210> 72

<211> 560

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (560)

<223> n = A,T,C or G

<400> 72

cctggacttg	tcttggttcc	agaacctgac	gaccggcgga	cgggcgacgtc	tcttttgact	60
aaaagacagt	gtccagtgtc	ccngcctagg	agtctacggg	gaccgcctcc	cgcgcccga	120
ccatgcccaa	cttctctggc	aactggaaaa	tcacccgac	ggaaaaacttc	gangaattgc	180
tcnaantgct	gggggtgaat	gtgatgctna	ngaanattgc	tgtggctgca	gcgtccaagc	240
cagcagtgga	gacnaacag	gaggagagaca	ctttctacat	caaaacctcc	accaccgtgc	300
gcaccacaaa	gattaacttc	nnngttgggg	aggantttga	ggancaaact	gtggatngga	360
ngcctgtnaa	aacctggtga	aatgggagaa	tganaataaa	atggtctgtg	ancanaaact	420
cctgaaagga	gaaggcccc	anaactcctg	gaccngaaaa	actgaccnc	cnatngggga	480
actgatnctt	gaacctgaa	cgggcgggat	ganccttttt	tnttgcencc	naanggggtc	540
tttccntttc	cccaaaaaaa					560

<210> 73

<211> 379

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (379)

<223> n = A,T,C or G

<400> 73

ctggggancc	ggcggtngc	nccatntcnn	gncgcgaagg	tggcaataaa	aanccnctga	60
aaccgcnaaa	naaacatgcc	naagatatgg	acgaggaaga	tnngctttc	nngnacaaanc	120
gnanngagga	acanaacaaa	ctcnangagc	tctcaagcta	atgccgcggg	gaagggggccc	180
ttggccacnn	gtggaattaa	gaaatctggc	aaanngtann	tgttccttgt	gcctnangag	240
ataagnagcc	ctttatttca	tctgtattta	aacctctctn	ttccctgnca	taacttcttt	300
tnccacgtan	agntggaant	anttggtgtc	ttggactgtt	gtncatttta	gannaaactt	360
ttgttcaaaa	aaaaaataa					379

<210> 74

<211> 437

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature
 <222> (1)...(437)
 <223> n = A,T,C or G

<400> 74
 actagttcag actgccacgc caaccccaga aaatacccca catgccagaa aagtgaagtc 60
 ctagggtgttt ccatctatgt ttcaatctgt ccatctacca ggctcgcga taaaaacaaa 120
 acaaaaaaac gctgccaggt tttanaagca gttctgggtct caaaaccatc aggatcctgc 180
 caccaggggt cttttgaaat agtaccacat gtaaaaggga atttggcttt cacttcatct 240
 aatcactgaa ttgtcaggct ttgattgata attgtagaaa taagtagcct tctgttgtgg 300
 gaataagtta taatcagtat tcatctcttt gttttttgtc actcttttct ctctnattgt 360
 gtcattttgta ctgtttgaaa aatattttctt ctataaaaatt aaactaacct gccttaaaaa 420
 aaaaaaaaaa aaaaaaa 437

<210> 75
 <211> 579
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(579)
 <223> n = A,T,C or G

<400> 75
 ctccgtcgcc gccaaagatga tgtgcggggc gccctcgcgc acgcagccgg ccaccgccga 60
 gaccagcac atcgccgacc aggtgaggtc ccagcttgaa gagaaagaaa acaagaagtt 120
 cctgtgtttt aaggccgtgt cattcaagag ccaggtggtc gcggggacaa actacttcat 180
 caaggtgcac gtcggcgacg aggacttcgt acacctgcga gtgttccaat ctctccctca 240
 tgaatacaag cccttgacct tatctaacta ccagaccaac aaagccaagc atgatgagct 300
 gacctatttc tgatcctgac ttgggacaag gcccttcagc cagaagactg acaaagtcatt 360
 cctccgtcta ccagagcgtg cacttgtgat cctaaaataa gtttcattct cgggctgtgc 420
 ccttgggggtg gaaggggcan gatctgcact gcttttgcat ttctcttctt aaatttcatt 480
 gtgttgattc ttctcttcca ataggtgatc ttnattactt tcagaatatt ttccaaatna 540
 gatatatattt naaaatcctt aaaaaaaaaa aaaaaaaaaa 579

<210> 76
 <211> 666
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(666)
 <223> n = A,T,C or G

<400> 76
 gtttatecta tctctccaac cagattgtca gtccttgag ggcaagagcc acagtatatt 60
 tccctgtttc ttccacagtg cctaataata ctgtggaact aggttttaata aattttttaa 120
 ttgatgttgt tatgggcagg atggcaacca gaccattgtc tcagagcagg tgctggctct 180
 ttcttggtta ctccatgttg gctagcctct ggtaacctct tacttattat cttcaggaca 240
 ctactacag ggaccagggg tgatgcaaca tccttgtctt tttatgacag gatgtttgct 300
 cagcttctcc aacaataaaa agcacgtggg aaaacacttg cggatattct ggactgtttt 360
 taaaaaatat acagtttacc gaaaatcata ttatcttaca atgaaaagga ntttatagat 420
 cagccagtga acaacctttt cccaccatac aaaaattcct tttcccgaan gaaaanggct 480

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ttctcaataa ncctcacttt cttaanatct tacaagatag ccccganac ttatcgaaac      540
tcatttttagg caaatatgan ttttattgtt cgttacttgt ttcaaaattt ggtattgtga      600
atatcaatta ccaccccat ctcccatgaa anaaangggg aanggtgaan ttcntaanccg      660
cttaaa                                         666

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<210> 77
<211> 396
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(396)
<223> n = A,T,C or G

```

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<400> 77
ctgcagcccg ggggatccac taatctacca nggttatttg gcagctaatt ctanatttgg      60
atcattgccc aaagttgcac ttgctggtct cttgggattt ggccttgga aggtatcata      120
catanganta tgccanaata aattccattt ttttgaaaat canctccttg gggctgggtt      180
tggtccacag cataacangc actgcctcct tacctgtgag gaatgcaaaa taaagcatgg      240
attaagtgag aagggagact ctcagccttc agcttcctaa attctgtgtc tgtgactttc      300
gaagtttttt aaacctctga atttgtacac atttaaaatt tcaagtgtac tttaaaataa      360
aatacttcta atgggaacaa aaaaaaaaaa aaaaaa                                         396

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<210> 78
<211> 793
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(793)
<223> n = A,T,C or G

```

```

<400> 78
gcacccctagc cgccgactca cacaaggcag gtgggtgagg aaatccagag ttgccatgga      60
gaaaattcca gtgtcagcat tcttgtctct tgtggccctc tcctacactc tggccagaga      120
taccacagtc aaacctggag ccaaaaagga cacaaggac tctcgacca aactgccccca      180
gaccctctcc agaggttggg gtgaccaact catctggact cagacatatg aagaagctct      240
atataaatcc aagacaagca acaaaccctt gatgattatt catcacttgg atgagtggcc      300
acacagtcna gctttaaaga aagtgtttgc tgaaaataaa gaaatccaga aattggcaga      360
gcagtttgtc ctctcaatc tggtttatga acaactgcac aaacacctt ctctgatgg      420
ccagtatgtc ccaggattat gtttgttgac ccatctctga cagttgaagc cgatatcctg      480
ggaagatatt cnaaccgtct ctatgcttac aaactgcaga tacgctctgt tgcttgacac      540
atgaaaaaagc tctcaagttg ctnaaaatga attgtaagaa aaaaaatctc cagccttctg      600
tctgtcggct tgaaaattga aaccagaaaa atgtgaaaaa tggctattgt ggaacanatn      660
gacacctgat taggttttgg ttatgttcac cactattttt aanaaaanan nttttaaaat      720
ttggttcaat tntctttttn aaacaatntg tttctacntt gnganctgat ttctaaaaaa      780
aataatnttt ggc                                         793

```

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<210> 79
<211> 456
<212> DNA
<213> Homo sapien

```

<220>
 <221> misc_feature
 <222> (1)...(456)
 <223> n = A,T,C or G

<400> 79
 actagtatgg ggtgggaggg cccacccttc tcccctaggg gctgttcttg ctccaaaggg 60
 ctccgtggag agggactggc agagctgang ccacctgggg ctggggatcc cactcttctt 120
 gcagctgttg agcgcaccta accactgggc atgccccac cctgctctc cgcacccgct 180
 tcctcccgac cccangacca ggctacttct cccctctctc tgctccctc ctgcccctgc 240
 tgctctgat cgtangaatt gangantgtc ccgccttggt gctganaatg gacagtggca 300
 ggggctggaa atgggtgtgt gtgtgtgtgt gtgtgtgtgt gtgtgtgtgt gcnccccccc 360
 tgcaagaccg agattgaggg aaancatgtc tgcctgggtg gaccatgttt cctctccata 420
 aantnccct gtgacnctca naaaaaaaaa aaaaaa 456

<210> 80
 <211> 284
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(284)
 <223> n = A,T,C or G

<400> 80
 ctttgtacct ctgaaaaaga taggtattgt gtcatgaaac ttgagtttaa attttatata 60
 taaaactaaa agtaatgtct acttttagcaa cacatactaa aattggaacc atactgagaa 120
 gaatagcatg acctccgtgc aaacaggaca agcaaatttg tgatgtgttg attaaaaaga 180
 aataaataaa tgtgtatatg tgtaacttgt atgtttatgt ggaatacaga ttgggaaata 240
 aaatgtattt cttactgtga aaaaaaaaaa aaaaaaaaaa aana 284

<210> 81
 <211> 671
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(671)
 <223> n = A,T,C or G

<400> 81
 gccaccaaca ttccaagcta ccctgggtac ctttgtgcag tagaagctag tgagcatgtg 60
 agcaagcggg gtgcacacgg agactcatcg ttataattta ctatctgcca agagtagaaa 120
 gaaaggctgg ggatatttgg gttggcttgg ttttgatttt ttgcttgttt gtttgtttgg 180
 tactaaaaca gtattatctt ttgaatatcg tagggacata agtatataca tgttatccaa 240
 tcaagatggc tagaatggtg cctttctgag tgtctaaaac ttgacacccc tggtaaatct 300
 ttcaacacac ttccactgcc tgcgtaatga agttttgatt catttttaac cactggaatt 360
 tttcaatgcc gtcattttca gttagatnat tttgcacttt gagattaaaa tgccatgtct 420
 atttgattag tcttattttt ttatttttac aggcattatca gtctcactgt tggctgtcat 480
 tgtgacaaag tcaaataaac ccccnaggac aacacacagt atgggatcac atattgtttg 540
 acattaagct ttggccaaaa aatgttgcac gtgttttacc tcgacttgct aaatcaatan 600
 canaaaggct ggctnataat gttggtggtg aaataattaa tnantaacca aaaaaaaaaa 660
 aaaaaaaaaa a 671

<210> 82
 <211> 217
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (217)
 <223> n = A,T,C or G

<400> 82
 ctgcagatgt ttcttgaatg ctttgtcaaa ttaanaaagt taaagtgcaa taatgtttga 60
 agacaataag tgggtggtgta tcttgtttct aataagataa acttttttgt ctttgcctta 120
 tcttattagg gagttgtatg tcagtgtata aaacatactg tgtggtataa caggcttaat 180
 aaattcttta aaaggaaaaa aaaaaaaaaa aaaaaaa 217

<210> 83
 <211> 460
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (460)
 <223> n = A,T,C or G

<400> 83
 cgcgagtggg agcaccagga tctcgggctc ggaacgagac tgcacggatt gttttaagaa 60
 aatggcagac aaaccagaca tgggggaaat cgccagcttc gatnaggcca agctgaanaa 120
 aacggagacg caggagaaga acaccctgcc gaccaaagag accattgagc angagaagcg 180
 gagtgaattt tctaagatc ctggaggatt tcttaccctc gtcctcttcg agaccccaat 240
 cgtgatgtgg aggaagagcc acctgcaaga tggacacgag ccacaagctg cactgtgaac 300
 ctgggcactc cgcgccgatg ccaccggcct gtgggtctct gaagggaccc cccccaatcg 360
 gactgccaaa ttctccggtt tgcctcggga tattatacaa nattatttgt atgaataatg 420
 annataaaac acacctcgtg gcancaaana aaaaaaaaaa 460

<210> 84
 <211> 323
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (323)
 <223> n = A,T,C or G

<400> 84
 tgggtgatct tggctctgtg gagctgctgg gacgggatct aaaagactat tctggaagct 60
 gtggtccaan gcattttgct ggcttaacgg gtcccgggaa aaaggacacc agctctctaa 120
 aattgaagtt taccganat aacaatcttt tgggcagaga tgcctatttt aacaaacncc 180
 gtccctgcgc aacaacnaac aatctctggg aaataccggc catgaacntg ctgtctcaat 240
 cnancatctc tctagctgac cgatcatatc gtcccagatt actacanatc ataataattg 300
 atttctgtgta naaaaaaaaa aaa 323

<210> 85
 <211> 771
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(771)
 <223> n = A,T,C or G

<400> 85
 aaactgggta ctcaacactg agcagatctg ttctttgagc taaaaacat gtgctgtacc 60
 aanagtttgc tcctggctgc tttgatgtca gtgctgtac tccacctctg cggcgaatca 120
 gaagcaagca actttgactg ctgtcttgga tacacagacc gtattcttca tcctaaattt 180
 attgtgggct tcacacggca gctggccaat gaaggctgtg acatcaatgc tatcatcttt 240
 cacacaaaga aaaagttgtc tgtgtgctga aatccaaaac agacttgggt gaaatatatt 300
 gtgcgtctcc tcagtaaaaa agtcaagaac atgtaaaaac tgtggctttt ctggaatgga 360
 attggacata gcccaagaac agaaagaact tgctgggggt ggagggtttca cttgcacatc 420
 atgganggtt tagtgcttat cttatttgtg ctcctgggac ttgtccaatt natgaagtta 480
 atcatattgc atcatanttt gctttgttta acatcacatt naaattaaac tgtattttat 540
 gttatttata gctntaggtt ttctgtgttt aactttttat acnaantttc cttaaactatt 600
 ttggtntant gcaanttaaa aattatatatt ggggggggaa taaatatagg antttctgca 660
 gccacaagct ttttttaaaa aaccantaca nccnngttaa atggtnggtc ccnaatgggt 720
 tttgcttttn antagaaaat ttnttagaac natttgaaaa aaaaaaaaaa a 771

<210> 86
 <211> 628
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(628)
 <223> n = A,T,C or G

<400> 86
 actagtttgc tttacatttt tgaaaagtat tatttttgtc caagtgttta tcaactaaac 60
 cttgtgttag gtaagaatgg aattttattaa gtgaatcagt gtgacccttc ttgtcataag 120
 attatcttaa agctgaagcc aaaatatgct tcaaaaagaaa angactttat tgttcattgt 180
 agttcataca ttcaaagcat ctgaactgta gtttctatag caagccaatt acatccataa 240
 gtggagaang aaatagatta atgtcnaagt atgattggtg gagggagcaa gggtgaagat 300
 aatctggggg tgaaattttc tagttttcat tctgtacatt tttagttnga catcagattt 360
 gaaatattaa tgtttacctt tcaatgtgtg gtatcagctg gactcantaa cacccttttc 420
 ttcctnnggg gatggggaat ggattattgg aaaatggaaa gaaaaaagta cttaaagcct 480
 tcctttcnca gtttctggct cctaccctac tgatttancc agaataagaa aacattttat 540
 catcntctgc tttattccca ttaatnaant tttgatgaat aaatctgctt ttatgcnnac 600
 ccaaggaatt nagtggnttc ntcttgtt 628

<210> 87
 <211> 518
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature

<222> (1)...(518)

<223> n = A,T,C or G

<400> 87

ttttttat	tttttagaga	gtagttcagc	ttttat	aaatttattg	cctgttttat	60
tataacaaca	ttatactgtt	tatggtttaa	tacatatggt	tcaaaatgta	taatacatca	120
agtagtacag	ttttaaaatt	ttatgcttaa	aacaagtttt	gtgtaaaaaa	tgcagataca	180
ttttacatgg	caaatacaatt	tttaagtcac	cctaaaaaatt	gatttttttt	tgaattttta	240
aaacacattt	aattttcaatt	tctctcttat	ataaccttta	ttactatagc	atggtttcca	300
ctacagttta	acaatgcagc	aaaattccca	tttcacggta	aattgggttt	taagcggcaa	360
ggttaaaatg	ctttgaggat	cctnaatacc	ctttgaactt	caaatagaag	ttatgggtgt	420
naatttaacc	ctcatgccat	aagcagaagc	acaagtttag	ctgcattttg	ctctaaactg	480
taaaancgag	ccccccgttg	aaaaagcaaa	agggaccc			518

<210> 88

<211> 1844

<212> DNA

<213> Homo sapien

<400> 88

gagacagtga	atcctagtat	caaaggattt	ttggcctcag	aaaaagttgt	tgattat	60
tattttat	tatttttcga	gactccgtct	caaaaaaaaa	aaaaaaaaaa	agaatcaca	120
ggatattgct	aaagcat	gagctgcttg	gaaaaaggga	agtagttgca	gtagagtttc	180
ttccatcttc	ttgggtgctgg	gaagccatat	atgtgtcttt	tactcaagct	aaggggtata	240
agcttatgtg	ttgaatttgc	tacatctata	tttcacatat	tctcacaata	agagaatttt	300
gaaatagaaa	tatcatagaa	cattttaagaa	agtttagtat	aaataatatt	ttgtgtgttt	360
taatcccttt	gaaggggatct	atccaaagaa	aatatttttac	actgagctcr	ttcctacacg	420
tctcagtaac	agatcctgtg	ttagtctttg	aaaatagctc	atttttttaa	tgtagtgag	480
tagatgtagc	atacatatga	tgtataatga	cgtgtattat	gttaacaatg	tctgcagatt	540
ttgtaggaat	acaaaacatg	gcctttttta	taagcaaaac	gggccaatga	ctagaataac	600
acatagggca	atctgtgaat	atgtattata	agcagcattc	cagaaaagta	gttgggtgaa	660
taattttcaa	gtcaaaaagg	gatatggaaa	gggaattatg	agtaacctct	attttttaag	720
ccttgctttt	aaattaaacg	ctacagccat	ttaaagccttg	aggataataa	agcttgagag	780
taataatgtt	agggttagcaa	agggttagat	gtatcacttc	atgcatgcta	ccatgatagt	840
aatgcagctc	ttcgagtcac	ttctggctac	tcaagatatt	cacccttttg	cccatagaaa	900
gcaccctacc	tcacctgctt	actgacattg	tcttagctga	tcacaagatc	attatcagcc	960
tccattat	cttactgtat	ataaaataca	gagttttata	ttttcctttc	ttcgtttttc	1020
accatattca	aaacctaaat	ttgtttttgc	agatggaatg	caaagtaatc	aagtgttcgt	1080
gctttcacct	agaaggggtg	ggctcctgaag	gaaagagggtc	cctaaatatc	ccccaccctg	1140
gggtgctcctc	cttccttggt	accctgacta	ccagaagtca	gggtgctagag	cagctggaga	1200
agtgcagcag	cctgtgcttc	cacagatggg	gggtgctgctg	caacaaggct	ttcaatgtgc	1260
ccatcttagg	gggagaagct	agatcctgtg	cagcagcctg	gtaagtcctg	aggaggttcc	1320
attgctcttc	ctgctgctgt	cctttgcttc	tcaacggggc	tcgctctaca	gtctagagca	1380
catgcagcta	acttgtgcct	ctgcttatgc	atgaggggta	aattaacaac	cataaccttc	1440
atttgaagtt	caaagggtgta	ttcaggatcc	tcaaagcatt	ttaaccttgc	cgcttaaaac	1500
ccaatttacc	gtgaaatggg	aattttgctg	cattgttaaa	ctgtagtgga	aaccatgcta	1560
tagtaataaa	ggttatataa	gagagaaatt	gaaattaaat	gtgtttttta	atttcaaaaa	1620
aaaatcaaatc	tttaggatga	cttaaaaatt	gatttgccat	gtaaaatgta	tctgcatttt	1680
ttacacaaaa	cttgttttta	gcataaaatt	ttaaaactgt	actacttgat	gtattataca	1740
ttttgaacca	tatgtattaa	accataaaca	gtataatgtt	gttataataa	aacaggcaat	1800
aaattttataa	ataaaagctg	aaaaaaaaaa	aaaaaaaaaa	aaaa		1844

<210> 89

<211> 523

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(523)

<223> n = A,T,C or G

<400> 89

tttttttttt	tttttttagt	caatccacat	ttattgatca	cttattatgt	accaggcact	60
gggataaaga	tgactgttag	tcactcacag	taaggaagaa	aactagcaaa	taagacgatt	120
acaatatgat	gtagaaaatg	ctaagccaga	gatatagaaa	ggtcctattg	ggtccttctg	180
tcacctgtgc	tttccacatc	cctacccttc	acaggccttc	cctccagctt	cctgcccccg	240
ctccccactg	cagatccccct	gggattttgc	ctagagctaa	acgagganat	gggccccctg	300
gccttgatga	gacttgaacc	caaccacaga	ctgggaaagg	gagcctttcg	anagtggatc	360
actttgatna	gaaaacacat	agggaattga	agagaaantc	cccaaattggc	caccctgtgt	420
ggtgctcaag	aaaagtgtgc	agaatggata	aatgaaggat	caagggaatt	aatanatgaa	480
taattgaatg	gtggctcaat	aagaatgact	ncnttgaatg	acc		523

<210> 90

<211> 604

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(604)

<223> n = A,T,C or G

<400> 90

ccagtgtggt	ggaatgcaaa	gattacccccg	gaagcttttcg	agaagctggg	attccctgca	60
gcaaaggaaa	tagccaatat	gtgtcgtttc	tatgaaatga	agccagaccg	agatgtcaat	120
ctcaccacc	aactaaatcc	caaagtcaaa	agcttcagcc	agtttatctc	agagaaccag	180
gggagccttc	aagggcatgt	agaaaatcag	ctgttcagat	aggcctctgc	accacacagc	240
ctctttcttc	tctgacccct	ttctctttta	cggcacaaca	ttcatgtttg	acagaacatg	300
ctggaatgca	attgtttgca	acaccgaagg	atttcctgcg	gtcgccctct	cagtaggaag	360
cactgcattg	gtgataggac	acggtaattt	gattcacatt	taacttgcta	gttagtgata	420
aggggtggta	cacctgtttg	gtaaaatgag	aagcctcgga	aacttgggag	cttctctcct	480
accactaatg	gggagggcag	attattactg	ggatttctcc	tggggtgaat	taatttcaag	540
ccctaattgc	tgaaattccc	ctnggcaggc	tccagttttc	tcaactgcat	tgcaaaattc	600
cccc						604

<210> 91

<211> 858

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(858)

<223> n = A,T,C or G

<400> 91

tttttttttt	ttttttttta	tgattattat	tttttttatt	gatctttaca	tcctcagtgt	60
tggcagagtt	tctgatgctt	aataaacatt	tgttctgata	agataagtgg	aaaaaattgt	120
catttcctta	ttcaagccat	gcttttctgt	gatattctga	tcctagttaga	acatacagaa	180

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ataaatgtct aaaacagcac ctcgattctc gtctataaca ggactaagtt cactgtgac 240
ttaaataaagc ttggctaaaa tgggacatga gtggaggtag tcacacttca gcgaagaaa 300
agaatctcct gtataatctc accaggagat tcaacgaatt ccaccacact ggactagtgg 360
atcccccggg ctgcaggaat tcgatatcaa gcttatcgat accgtcgacc tcgagggggg 420
gcccgggtacc caattcgccc tatagtgagt cgtattacgc gcgctcactg gccgtcgttt 480
tacaacgtcg tgactgggaa aacctggcg ttaccaact taatcgctt gcagcacatc 540
cccccttcgc cagctggcgt aatagcgaan agcccgacc gatcgccctt ncaacagttg 600
cgcagcctga atggcgaatg ggacgcgcc tgtagcggcg cattaaagcg cggcnggggtg 660
tggnggntcc ccacgtgac cgntacactt ggcagcgct tacgcccgtc ntctgctttc 720
ttcccttctt ttctcgacc gtctcgccgg tttccccgnn agctnttaat cgggggnctc 780
cctttanggg tncnaattaa nggnttaacn gaccttngan cccaaaaact ttgattaggg 840
ggaaggtccc cgaagggg 858

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```

<210> 92
<211> 585
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(585)
<223> n = A,T,C or G

```

```

<400> 92
gttgaatctc ctggtgagat tatacaggag attctctttc ttcgctgaag tgtgactacc 60
tccactcatg tcccatttta gccaaagctta ttttaagatca cagtgaactt agtcctgtta 120
tagacgagaa tcgaggtgct gtttttagaca tttatttctg tatgttcaac taggatcaga 180
atatcacaga aaagcatggc ttgaataagg aatgacaat tttttccact tatctgatca 240
gaacaaatgt ttattaagca tcagaaactc tgccaacact gaggatgtaa agatcaataa 300
aaaaaataat aatcatnann naaanannan nngaaggggc gccgccaccg cggtgaggct 360
ccagcttttg ttcccttttag tgaggggttaa ttgcgcgctt ggcgttaatc atgggtcatag 420
ctgtttcctg tgtgaaattg ttatccggct cacaattccn cncaacatac gagccgggaa 480
gcntnangtg taaaagcctg ggggtgccta attgagttag ctnactcaca ttaattgngt 540
tgcgctccac ttgcccgcct ttccantccg ggaaacctgt tcgnc 585

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```

<210> 93
<211> 567
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(567)
<223> n = A,T,C or G

```

```

<400> 93
cggcagtgtt gctgtctgcg tgtccacctt ggaatctggc tgaactggct gggaggacca 60
agactgcggc tgggggtggc anggaaggga accgggggct gctgtgaagg atcttggaac 120
ttccctgtac ccaccttccc cttgcttcat gtttgtnag gaaccttgtg ccggccaagc 180
ccagtttctt tgtgtgatac actaatgtat ttgctttttt tgggaaatan anaaaaatca 240
attaaattgc tantgtttct ttgaannnnn nnnnnnnnnn nnnnnnnggg ggggncgccc 300
ccnccgngga aacnccccct tttgttccct ttaattgaaa ggttaattng cncnctggc 360
gttaancnt gggccaaanc tngttncccg tgntgaaatt gtnatcccc tcccaaattc 420
cccccncc ttccaaaccc ggaaancctn annntgttna ancccggggg gttgcctaan 480
ngnaattnaa ccnaaccccc nttaaatng nntttgcn cnccnngccc cnccttccca 540

```

nttcggggaa aacctntcc gtgccca

567

<210> 94
 <211> 620
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(620)
 <223> n = A,T,C or G

<400> 94
 actagtcaaa aatgctaaaa taatttgga gaaaatattt ttaagtagt gttatagttt 60
 catgtttatc ttttattatg ttttgtgaag ttgtgtcttt tcactaatta cctatactat 120
 gccaatattt ccttatatct atccataaca tttatactac atttgtaana naatatgcac 180
 gtgaaactta acactttata aggtaaaaat gaggtttcca anatttaata atctgatcaa 240
 gttcttggtta tttccaaata gaatggactt ggtctgttaa gggctaagga gaagaggaag 300
 ataagggttaa aagttgttaa tgaccaaaca ttctaaaaga aatgcaaaaa aaaagtttat 360
 tttcaagcct tcgaactatt taaggaaagc aaaatcattt cctaaatgca tatcatttgt 420
 gagaatttct cattaatatt ctgaatcatt catttcacta aggctcatgt tnactccgat 480
 atgtctctaa gaaagtacta tttcatgggc caaacctggg tgccatantt gggtaaaggc 540
 tttcccttaa gtgtgaaant atttaaaatg aaattttcct ctttttataa attctttana 600
 aggggttaagg gtgttgaggga 620

<210> 95
 <211> 470
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(470)
 <223> n = A,T,C or G

<400> 95
 ctgcaccttc tctgcacagc ggatgaaccc tgagcagctg aagaccagaa aagccactat 60
 nactttntgc ttaattcang agcttacang attcttcaaa gagtgngtcc agcatccttt 120
 gaaacatgag ttcttaccag cagaagcaga cctttacccc accacctcag cttcaacagc 180
 agcaggtgaa acaacccatc cagcctccac ctnaggaaat atttggtccc acaaccaagg 240
 agccatgcc acaaaagggt ccacaacctg naaacacaaa nattccagag ccaggctgta 300
 ccaaggctcc tgagccaggg ctgtaccaan gtccctgagc cagggtgtac caangtccct 360
 gagccaggat gtaccaaggc ccctgancca gggtgtccaa ggtccctgag ccaggctaca 420
 ccaagggcct gngccaggca gcatcaangt ccctgaccaa ggcttatcaa 470

<210> 96
 <211> 660
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(660)
 <223> n = A,T,C or G

<400> 96
 tttttttttt tttttttttt ggaattaaaa gcaatttaaat gagggcagag caggaaacat 60
 gcatttcctt tcattcgaat cttcagatga accctgagca gccgaagacc agaaaagcca 120
 tgaagacttt ctgcttaatt caggggctta caggattctt cagagtgtgt gtgaacaaaa 180
 gctttatagt acgtattttt aggatacaaa taagagagag actatggctt ggggtgagaa 240
 tgtactgatt acaaggctta cagacaatta agacacagaa acagatggga agagggtgnc 300
 cagcatctgg nggttggtt ctcaagggtt tgtctgtgca ccaaattact tctgcttggn 360
 cttctgctga gctgggctt gagtgaccgt tgaaggacat ggctctggta cctttgtgta 420
 gcctgncaca ggaactttgg tgtatccttg ctcagggaact ttgatggcac ctggctcagg 480
 aaacttgatg aagccttggg caagggacct tgatgcttgc tggctcaggg accttgngn 540
 ancctgggct canggacct tgnncnaacc ttggcttcaa gggacccttg gnacatcctg 600
 gcnnagggac ccttggggcc aaccctgggc ttnagggacc ctttggnntnc nanccttggc 660

<210> 97
 <211> 441
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(441)
 <223> n = A,T,C or G

<400> 97
 gggaccatac anagtattcc tctcttcaca ccaggaccag ccactgttgc agcatgagtt 60
 cccagcagca gaagcagccc tgcacccac cccctcagct tcagcagcag caggtgaaac 120
 agccttgcca gcctccacct caggaacct gcaccccaa aaccaaggag ccctgccacc 180
 ccaagggtgcc tgagccctgc cccccaaag tgcttgagcc ctgccagccc aaggttccag 240
 agccatgcca cccaagggtg cctgagccct gcccttcaat agtcaactcca gcaccagccc 300
 agcagaanac caagcagaag taatgtgggt cacagccatg cctttagagga gccggccacc 360
 agatgctgaa tcccctatcc cattctgtgt atgagtccca tttgccttgc aattagcatt 420
 ctgtctcccc caaaaaaaaaa a 441

<210> 98
 <211> 600
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(600)
 <223> n = A,T,C or G

<400> 98
 gtattcctct cttcacacca ggaccagcca ctgttgcagc atgagttccc agcagcagaa 60
 gcagccctgc atcccacccc ctcagcttca gcagcagcag gtgaaacagc cttgccagcc 120
 tccacctcag gaacctatgca tccccaaaac caaggagccc tgccaccca aggtgcctga 180
 gccctgccac cccaaagtgc ctgagccctg ccagcccaag gttccagagc catgccaccc 240
 caagggtgct gagccctgcc cttcaatagt cactccagca ccagcccagc agaanaccaa 300
 gcagaagtaa tgtggtccac agccatgccc ttgaggagcc ggccaccana tgctgaatcc 360
 cctatcccat tctgtgtatg agtcccattt gccttgcaat tagcattctg tctcccccaa 420
 aaaagaatgt gctatgaagc tttctttcct acacactctg agtctctgaa tgaagctgaa 480
 ggtcttaant acaganctag ttttcagctg ctcagaattc tctgaagaaa agattttaaga 540
 tgaaaggcaa atgattcagc tccttattac cccattaaat tcnctttcaa ttccaaaaaa 600

<210> 99
 <211> 667
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (667)
 <223> n = A,T,C or G

<400> 99
 actagtgtgact gagttcctgg caaagaaatt tgacctggac cagttgataa ctcattgtttt 60
 accattttaaa aaaatcagtg aaggatttga gctgctcaat tcaggacaaa gcattcgaac 120
 ggtcctgacg ttttgagatc caaagtggca ggaggtctgt gttgtcatgg tgaactggag 180
 tttctcttgt gagagttccc tcatctgaaa tcatgtatct gtctcacaaa tacaagcata 240
 agtagaagat ttgttgaaga catagaaccc ttataaagaa ttattaacct ttataaacat 300
 ttaaagtcct gtgagcacct gggaattagt ataataacaa tgttnatatt ttgtatttac 360
 attttgttaag gctataattg tatcttttaa gaaaacatac cttggatttc tatgttgaaa 420
 tggagatttt taagagtttt aaccagctgc tgcagatata ttactcaaaa cagatatagc 480
 gtataaagat atagtaaag catctcctag agtaatatcc acttaacaca ttggaaacta 540
 ttatttttta gatttgaata tnaatgttat tttttaaaca cttgttatga gttacttggg 600
 attacatttt gaaatcagtt cattccatga tgcanattac tgggattaga ttaagaaaga 660
 cggaaaaa 667

<210> 100
 <211> 583
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (583)
 <223> n = A,T,C or G

<400> 100
 gttttgtttg taagatgatc acagtcattg tacactgatc taaaggacat atatataacc 60
 ctttaaaaaa aaaatcactg cctcattctt atttcaagat gaatttctat acagactaga 120
 tgtttttctg aagatcaatt agacattttg aaaaatgattt aaagtgtttt ccttaatgtt 180
 ctctgaaaac aagtttcttt tgtagtttta accaaaaaag tgcccttttt gtcactggat 240
 tctcctagca ttcattgattt ttttttcata caatgaaatt aaaattgcta aaatcatgga 300
 ctggctttct ggttggattt caggtaagat gtgtttaagg ccagagcttt tctcagtatt 360
 tgattttttt ccccaatatt tgatttttta aaaaatatata catnggtgct gcatttatat 420
 ctgctgggtt aaaattctgt catatttcac ttctagcctt ttagttatgg caaatcatat 480
 tttactttta cttaaagcat ttggtnattt ggantatctg gttctannct aaaaaaanta 540
 attctatnaa ttgaantttt ggtactcnnc catattttgga tcc 583

<210> 101
 <211> 592
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (592)
 <223> n = A,T,C or G

<400> 101

gtggagacgt	acaaagagca	gccgctcaag	acacctggga	agaaaaagaa	aggcaagccc	60
gggaaacgca	aggagcagga	aaagaaaaaa	cggcgaactc	gctctgcctg	gttagactct	120
ggagtgcactg	ggagtgggct	agaaggggac	cacctgtctg	acacctccac	aacgtcgctg	180
gagctcgatt	cacggaggca	ttgaaatfff	cagcaganac	cttccaagga	catattgcag	240
gattctgtaa	tagtgaacat	atggaaagta	ttagaaatat	ttattgtctg	taaatactgt	300
aaatgcattg	gaataaaact	gtctcccca	ttgctctatg	aaactgcaca	ttggtcattg	360
tgaatatttt	tttttttgcc	aaggctaate	caattattat	tatcacattt	accataattt	420
atftttgtcca	ttgatgtatt	tattttgtaa	atgtatcttg	gtgctgctga	atttctatat	480
ttttgtaca	taatgcnttt	anatatacct	atcaagtttg	ttgataaatg	acncaatgaa	540
gtgnncnncn	ttggngggtg	aatttaatga	atgcctaatt	ttattatccc	aa	592

<210> 102

<211> 587

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (587)

<223> n = A,T,C or G

<400> 102

cgctctaagc	acttagacta	catcagggaa	gaacacagac	cacatccctg	tcctcatgcg	60
gcttatgttt	tctggaagaa	agtggagacc	nagtccttgg	ctttagggct	ccccggctgg	120
gggctgtgca	ntccggtcag	ggcgggaagg	gaaatgcacc	gctgcatgtg	aacttacagc	180
ccaggcggat	gccccctccc	ttagcactac	ctggcctcct	gcatccccc	gcctcatgtt	240
cctcccacct	tcaaanaatg	aanaacccca	tgggcccagc	cccttgccct	ggggaaccaa	300
ggcagccttc	caaaactcag	gggctgaagc	anactattag	ggcaggggct	gactttgggt	360
gacactgccc	attccctctc	agggcagctc	angtcaccen	ggnetcttga	accagcctg	420
ttcctttgaa	aaagggcaaa	actgaaaagg	gcttttccca	naaaaagaaa	aaccagggaa	480
ctttgccagg	gcttcnntnt	taccaaaach	ncttctcnng	gatttttaat	tccccattng	540
gcctccactt	accnggggcn	atgccccaaa	attaanaatt	tcccatc		587

<210> 103

<211> 496

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (496)

<223> n = A,T,C or G

<400> 103

anaggactgg	ccctacntgc	tctctctcgt	cctacctatc	aatgcccaac	atggcagaac	60
ctgcanccct	tggncactgc	anatggaaac	ctctcagtgt	cttgacatca	ccctaccnt	120
gcggtgggtc	tccaccacaa	ccactttgac	tctgtgtgcc	ctgnanggtg	gnttctcctg	180
actggcagga	tggaccttan	ccnacatata	cctctgttcc	ctctgctnag	anaaagaatt	240
cccttaacat	gatataatcc	acccatgcaa	ntngctactg	gccagctac	catttaccat	300
ttgcctacag	aatttcattc	agtctacact	ttggcattct	ctctggcgat	agagtgtggc	360
tgggctgacc	gcaaaagggtg	ccttacacac	tggccccccac	cctcaaccgt	tgacncatca	420
gangcttgcc	tctctcttct	gattnncccc	catgttggat	atcaggggtgc	tcnagggatt	480
ggaaaagaaa	caaaac					496

<210> 104
 <211> 575
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(575)
 <223> n = A,T,C or G

```

<400> 104
gcacctgctc tcaatccnnc tctcaccatg atcctccgcc tgcanaaaact cctctgccaa      60
ctatggangt ggtttcnggg gtggetcttg ccaactggga agaagccgtg gtgtctctac      120
ctgttcaact cngtttgtgt ctgggggatc aactnggggc tatggaagcg gctnaactgt      180
tgttttggtg gaagggctgg taattggctt tgggaagtng cttatngaag ttggcctnng      240
gaagttgcta ttgaaagtng ccntggaagt ngntttggtg gggggttttg ctggtggcct      300
ttgttnaatt tgggtgcttt gtnaatggcg gccccctcnc ctgggcaatg aaaaaaatca      360
ccnatgcngn aaacctcnac nnaacagcct gggcttcctc cacctcgaaa aaagttgctc      420
cccccccaaa aaaggncaan cccctcaann tgggaangttg aaaaaatcct cgaatgggga      480
nccnnaaaac aaaaancccc ccntttcccn gnaanggggg aaataccncc cccccactta      540
cnaaaacctt tntaaaaaac cccccgggaa aaaaaa      575

```

<210> 105
 <211> 619
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(619)
 <223> n = A,T,C or G

```

<400> 105
cactagtagg atagaaacac tgtgtcccga gagtaaggag agaagctact attgattaga      60
gcctaaccce ggttaactgc aagaagaggg gggatacttt cagctttcca tgtaactgta      120
tgcataaagc caatgtagtc cagttttctaa gatcatgttc caagctaact gaatcccact      180
tcaatacaca ctcatgaact cctgatggaa caataacagg cccaagcctg tggatatgatg      240
tgcacacttg ctagactcan aaaaaatact actctcataa atgggtggga gtattttggt      300
gacaacctac tttgcttggc tgagtgaagg aatgatattc atatattcat ttattccatg      360
gacatttagt tagtgctttt tatataccag gcatgatgct gagtgacact cttgtgtata      420
tttccaaatt tttgtacagt cgctgcacat atttgaaatc atatattaag acttccaaaa      480
aatgaagtcc ctgggttttc atggcaactt gatcagtaaa ggattcncct ctgtttggtgta      540
cttaaaacat ctactatatn gttnanatga aattcctttt cccnccctcc cgaaaaaana      600
aagtgggtgg gaaaaaaa      619

```

<210> 106
 <211> 506
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(506)
 <223> n = A,T,C or G

```

<400> 106
cattggtntct ttcatttgct ntggaagtgt nnatctctaa cagtggacaa agttcccngt      60
gccttaaact ctgtnacact tttgggaant gaaaanttng tantatgata ggttattctg      120
angtanagat gttctggata ccattanatn tgccccnngt gtcagaggct catattgtgt      180
tatgtaaatg gtatntcatt cgctactatn antcaattng aaatanggtc tttgggttat      240
gaatantnng cagcncanct nanangetgt ctgtngtatt cattgtgggc atagcacctc      300
acancattgt aacctcnaic nagtgagaca nactagnaan ttcctagtga tggctcanga      360
ttccaaatgg nctcatntcn aatgttttaa agttanttaa gtgtaagaaa tacagactgg      420
atgttccacc aactagtacc tgtaatgaacn ggctgtgccc aacacatctc ccttttccat      480
gactgtggta ncccgcacg gaaaaa                                506

```

```

<210> 107
<211> 452
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(452)
<223> n = A,T,C or G

```

```

<400> 107
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tcttttgaag catagataat attgtttggg aaatgtttct tttgtttggg aaatgtttct      120
tttaaagacc ctctattct ataaaactct gcatgtagag gcttgtttac ctttctctct      180
ctaaggttta caataggagt ggtgatttga aaaatataaa attatgagat tgggttttct      240
gtggcataaa ttgcatcact gtatcatttt cttttttaac cggtaagant ttcagtttgt      300
tggaaaagtaa ctgtganaac ccagtttccc gtccatctcc cttagggact acccatagaa      360
catgaaaagg tccccacnga agcaagaaga taagtctttc atggctgctg gttgcttaaa      420
ccacttttaa accaaaaaat tccccttggg aa                                452

```

```

<210> 108
<211> 502
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(502)
<223> n = A,T,C or G

```

```

<400> 108
atcttcttcc cttaattagt tnttattttat ntattaaatt ttattgcatg tcctggcaaa      60
caaaaagaga ttgtagattg gcttctgggt ccccaaaagc ccataacaga aagtaccaca      120
agaccncaac tgaagcttaa aaaatctatc acatgtataa tacctttnga agaacattaa      180
tanagcatat aaaactttta acatntgctt aatgttgtnc aattataaaa ntaatngaaa      240
aaaatgtccc tttaacatnc aatatccac atagtgttat tttaggggat taccnngnaa      300
naaaaaaagg gtagaaggga tttaatgaaa actctgcttn ccatttctgt ttanaaacgt      360
ctccagaaca aaaacttntc aantctttca gctaaccgca tttgagctna ggccactcaa      420
aaactccatt agnccactt tctaanggtc tctanagctt actaancctt ttgacccctt      480
accctggnta ctctgccct ca                                502

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```

<210> 109
<211> 1308

```

<212> DNA

<213> Homo sapien

<400> 109

```

acccgaggtc tcgctaaaat catcatggat tcacttggcg ccgtcagcac tcgacttggg      60
tttgatcttt tcaaagagct gaagaaaaca aatgatggca acatcttctt ttcccctgtg      120
ggcatcttga ctgcaattgg catggtcctc ctggggaccc gaggagccac cgcttcccag      180
ttggaggagg tgtttcactc tgaaaaagag acgaagagct caagaataaa ggctgaagaa      240
aaagaggtga ttgagaacac agaagcagta catcaacaat tccaaaagtt tttgactgaa      300
ataagcaaac tactaatga ttatgaactg aacataacca acaggctgtt tggagaaaaa      360
acatacctct tccttcaaaa atacttagat tatgttgaaa aatattatca tgcattctctg      420
gaacctgttg attttgtaaa tgcagccgat gaaagtcgaa agaagattaa ttccctgggtt      480
gaaagcaaaa caaatgaaaa aatcaaggac ttgttcccag atggctctat tagtagctct      540
accaagctgg tgctgggtgaa catggtttat tttaaagggc aatgggacag ggagtttaag      600
aaagaaaata ctaaggaaga gaaattttgg atgaataaga gcacaagtaa atctgtacag      660
atgatgacac agagccattc ctttagcttc actttcctgg aggacttgca ggccaaaatt      720
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agttacgata tagaggcggt cctggctgcc atggggatgg gcgatgcctt cagtgcacac      960
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agttcctttg tggcagtaac tgaggaaggc accgaggctg cagctgccac tggcataggc      1080
tttactgtca catccgcccc aggtcatgaa aatgttcaact gcaatcatcc cttcctgttc      1140
ttcatcaggc acaatgaatc caacagcatc ctcttcttcg gcagattttc ttctccttaa      1200
gatgatcgtt gccatggcat tgctgctttt agcaaaaaac aactaccagt gttactcata      1260
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```

<210> 110

<211> 391

<212> PRT

<213> Homo sapien

<400> 110

```

Met Asp Ser Leu Gly Ala Val Ser Thr Arg Leu Gly Phe Asp Leu Phe
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Lys Glu Leu Lys Lys Thr Asn Asp Gly Asn Ile Phe Phe Ser Pro Val
          20          25          30
Gly Ile Leu Thr Ala Ile Gly Met Val Leu Leu Gly Thr Arg Gly Ala
          35          40          45
Thr Ala Ser Gln Leu Glu Glu Val Phe His Ser Glu Lys Glu Thr Lys
          50          55          60
Ser Ser Arg Ile Lys Ala Glu Glu Lys Glu Val Ile Glu Asn Thr Glu
65          70          75          80
Ala Val His Gln Gln Phe Gln Lys Phe Leu Thr Glu Ile Ser Lys Leu
          85          90          95
Thr Asn Asp Tyr Glu Leu Asn Ile Thr Asn Arg Leu Phe Gly Glu Lys
          100          105          110
Thr Tyr Leu Phe Leu Gln Lys Tyr Leu Asp Tyr Val Glu Lys Tyr Tyr
          115          120          125
His Ala Ser Leu Glu Pro Val Asp Phe Val Asn Ala Ala Asp Glu Ser
          130          135          140
Arg Lys Lys Ile Asn Ser Trp Val Glu Ser Lys Thr Asn Glu Lys Ile
          145          150          155          160
Lys Asp Leu Phe Pro Asp Gly Ser Ile Ser Ser Ser Thr Lys Leu Val
          165          170          175

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Leu Val Asn Met Val Tyr Phe Lys Gly Gln Trp Asp Arg Glu Phe Lys
 180 185 190
 Lys Glu Asn Thr Lys Glu Glu Lys Phe Trp Met Asn Lys Ser Thr Ser
 195 200 205
 Lys Ser Val Gln Met Met Thr Gln Ser His Ser Phe Ser Phe Thr Phe
 210 215 220
 Leu Glu Asp Leu Gln Ala Lys Ile Leu Gly Ile Pro Tyr Lys Asn Asn
 225 230 235 240
 Asp Leu Ser Met Phe Val Leu Leu Pro Asn Asp Ile Asp Gly Leu Glu
 245 250 255
 Lys Ile Ile Asp Lys Ile Ser Pro Glu Lys Leu Val Glu Trp Thr Ser
 260 265 270
 Pro Gly His Met Glu Glu Arg Lys Val Asn Leu His Leu Pro Arg Phe
 275 280 285
 Glu Val Glu Asp Ser Tyr Asp Leu Glu Ala Val Leu Ala Ala Met Gly
 290 295 300
 Met Gly Asp Ala Phe Ser Glu His Lys Ala Asp Tyr Ser Gly Met Ser
 305 310 315 320
 Ser Gly Ser Gly Leu Tyr Ala Gln Lys Phe Leu His Ser Ser Phe Val
 325 330 335
 Ala Val Thr Glu Glu Gly Thr Glu Ala Ala Ala Ala Thr Gly Ile Gly
 340 345 350
 Phe Thr Val Thr Ser Ala Pro Gly His Glu Asn Val His Cys Asn His
 355 360 365
 Pro Phe Leu Phe Phe Ile Arg His Asn Glu Ser Asn Ser Ile Leu Phe
 370 375 380
 Phe Gly Arg Phe Ser Ser Pro
 385 390

<210> 111

<211> 1419

<212> DNA

<213> Homo sapien

<400> 111

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ggcgccgtca	gcactcgact	tgggtttgat	cttttcaaag	agctgaagaa	aacaaatgat	180
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attgagaaca	cagaagcagt	acatcaacaa	ttccaaaagt	ttttgactga	aataagcaaa	420
ctcactaatg	attatgaact	gaacataacc	aacaggctgt	ttggagaaaa	aacatacctc	480
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gattttgtaa	atgcagccga	tgaaagtcga	aagaagatta	attcctgggt	tgaaagcaaa	600
acaaatgaaa	aaatcaagga	cttggtccca	gatggctcta	ttagtagctc	taccaagctg	660
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cagatgccatt	cctttagctt	cactttcctg	gaggacttgc	aggccaaaat	tctagggatt	840
ccatataaaa	acaacgacct	aagcatgttt	gtgcttctgc	ccaacgacat	cgatggcctg	900
gagaagataa	tagataaaaat	aagtcctgag	aaattggtag	agtggaactg	tccagggcat	960
atggaagaaa	gaaaggtgaa	tctgcacttg	ccccggtttg	aggtggagga	cagttacgat	1020
ctagaggcgg	tcttggtctg	catggggatg	ggcgatgcct	tcagttagca	caaagccgac	1080
tactcgggaa	tgctcgtcagg	ctccgggttg	tacgcccaga	agttcctgca	cagttccttt	1140
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acatccgccc caggatcatga aaatgttcac tgcaatcatc ccttccctggt cttcatcagg 1260
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<210> 112
<211> 400
<212> PRT
<213> Homo sapien

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<400> 112
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Gly Ile Leu Thr Ala Ile Gly Met Val Leu Leu Gly Thr Arg Gly Ala
 35     40     45
Thr Ala Ser Gln Leu Glu Glu Val Phe His Ser Glu Lys Glu Thr Lys
 50     55     60
Ser Ser Arg Ile Lys Ala Glu Glu Lys Glu Val Val Arg Ile Lys Ala
 65     70     75     80
Glu Gly Lys Glu Ile Glu Asn Thr Glu Ala Val His Gln Gln Phe Gln
 85     90     95
Lys Phe Leu Thr Glu Ile Ser Lys Leu Thr Asn Asp Tyr Glu Leu Asn
100    105    110
Ile Thr Asn Arg Leu Phe Gly Glu Lys Thr Tyr Leu Phe Leu Gln Lys
115    120    125
Tyr Leu Asp Tyr Val Glu Lys Tyr Tyr His Ala Ser Leu Glu Pro Val
130    135    140
Asp Phe Val Asn Ala Ala Asp Glu Ser Arg Lys Lys Ile Asn Ser Trp
145    150    155    160
Val Glu Ser Lys Thr Asn Glu Lys Ile Lys Asp Leu Phe Pro Asp Gly
165    170    175
Ser Ile Ser Ser Ser Thr Lys Leu Val Leu Val Asn Met Val Tyr Phe
180    185    190
Lys Gly Gln Trp Asp Arg Glu Phe Lys Lys Glu Asn Thr Lys Glu Glu
195    200    205
Lys Phe Trp Met Asn Lys Ser Thr Ser Lys Ser Val Gln Met Met Thr
210    215    220
Gln Ser His Ser Phe Ser Phe Thr Phe Leu Glu Asp Leu Gln Ala Lys
225    230    235    240
Ile Leu Gly Ile Pro Tyr Lys Asn Asn Asp Leu Ser Met Phe Val Leu
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Leu Pro Asn Asp Ile Asp Gly Leu Glu Lys Ile Ile Asp Lys Ile Ser
260    265    270
Pro Glu Lys Leu Val Glu Trp Thr Ser Pro Gly His Met Glu Glu Arg
275    280    285
Lys Val Asn Leu His Leu Pro Arg Phe Glu Val Glu Asp Ser Tyr Asp
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305    310    315    320
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<211> 957
<212> DNA
<213> Homo sapien
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<400> 113						
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<210> 114
<211> 161
<212> PRT
<213> Homo sapien
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150

155

160

<210> 115
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<212> DNA
<213> Homo sapien

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<212> DNA
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<210> 117

<211> 6921

<212> DNA

<213> Homo sapien

<400> 117

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<400> 119

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<210> 123

<211> 2294

<212> DNA

<213> Homo sapien

<400> 123

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<210> 124

<211> 956

<212> DNA

<213> Homo sapien

<400> 124

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<210> 125

<211> 486

<212> DNA

<213> Homo sapien

<220>

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<222> (1)...(486)

<223> n = A,T,C or G

<400> 125

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<210> 126
 <211> 3552
 <212> DNA
 <213> Homo sapien

<400> 126						
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<210> 127

<211> 754

<212> DNA

<213> Homo sapien

<400> 127

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<210> 128

<211> 374

<212> DNA

<213> Homo sapien

<400> 128

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<210> 129

<211> 546

<212> DNA

<213> Homo sapien

<400> 129

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<210> 130

<211> 5156

<212> DNA

<213> Homo sapien

<400> 130

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<210> 131

<211> 671

<212> DNA

<213> Homo sapien

<400> 131

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<210> 132

<211> 590

<212> DNA

<213> Homo sapien

<400> 132

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<210> 133

<211> 581

<212> DNA

<213> Homo sapien

<400> 133

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<210> 134

<211> 4797

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

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<223> n = A,T,C or G

<400> 134

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<210> 135

<211> 2856

<212> DNA

<213> Homo sapien

<400> 135

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tttgatccct	gttaccacaga	gaatatatac	attctttatc	ttgacattca	aggcatttct	2760
atcacatatt	tgatagtgtg	tgttcaaaaa	aacactagtt	ttgtgccagc	cgtgatgctc	2820
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<210> 136

<211> 356

<212> DNA

<213> Homo sapien

<400> 136

ggtggagcca	aatgaagaaa	atgaagatga	aagagacaga	cacctcagtt	tttctggatc	60
aggcattgat	gatgatgaag	attttatctc	cagcaccatt	tcaaccacac	cacgggcttt	120
tgaccacaca	aaacagaacc	aggactggac	tcagtggaac	ccaagccatt	caaatccgga	180
agtgtacttt	cagacaacca	caaggatgac	tgatgtagac	agaaatggca	ccactgctta	240
tgaaggaaac	tggaacccag	aagcacaccc	tccctcatt	caccatgagc	atcatgagga	300
agaagagacc	ccacattcta	caagcacaat	ccaggcaact	cctagtagta	caacgg	356

<210> 137

<211> 356

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (356)

<223> n = A,T,C or G

<400> 137

gcaggtggag	aagacatttt	attgttcctg	gggtctctgg	aggcccattg	gtggggctgg	60
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gtcactggct	gcccccgaa	cagggcgctg	ctccatggct	ctgcttgtgg	tagtctgtgg	120
ctatgtctcc	cagcaaggac	agaaactcag	aaaaatcaat	cttcttatcc	tcattcttgt	180
cctttttctc	aaagacatcg	gcgaggtaat	ttgtgccctt	tttacctcgg	cccgcgacca	240
cgctaaggcc	aaanttccag	acanayggcc	gggcgggtnc	nataggggan	cccaacttgg	300
ggacccaaac	tctggcgcg	aaacacangg	gcataagctt	gnttcctgtg	gggaaa	356

<210> 138

<211> 353

<212> DNA

<213> Homo sapien

<400> 138

aggtccagtc	ctccacttgg	cctgatgaga	gtggggagtg	gcaaggggacg	tttctcctgc	60
aatagacact	tagatttctc	tcttgtggga	agaaaccacc	tgcccatcca	ctgactcttc	120
tacattgatg	tggaaattgc	tgctgctacc	accacctcct	gaagaggctt	ccctgatgcc	180
aatgccagcc	atcttggcat	cctggccctc	gagcaggctg	cggtaagtag	cgatctcctg	240
ctccagccgt	gtctttatgt	caagcagcat	cttgtactcc	tggttctgag	cctccatctc	300
gcacgggagc	tcactcagac	ctcgscgsg	mssmcgctam	gccgaattcc	agc	353

<210> 139

<211> 371

<212> DNA

<213> Homo sapien

<400> 139

agcgtgggtcg	cggccgaggt	ccatccgaag	caagattgca	gatggcagtg	tgaagagaga	60
agacatatctc	tacacttcaa	agctttgggtg	caattcccat	cgaccagagt	tggtccgacc	120
agccttggaa	aggtcactga	aaaatcttca	attggattat	gttgacctct	accttattca	180
ttttccagtg	tctgtaaaagc	caggtgagga	agtgatccca	aaagatgaaa	atggaaaaat	240
actatttgac	acagtggatc	tctgtgccac	gtgggaggcc	gtggagaagt	gtaaagatgc	300
aggattggac	ctgcccgggc	ggccgctcga	aagccgaatt	ccagcacact	ggcgcccggt	360
actagtggat	c					371

<210> 140

<211> 370

<212> DNA

<213> Homo sapien

<400> 140

tagcgtgggtc	gcggccgagg	tccatctccc	tttgggaact	agggggctgc	tggtgggaaa	60
tgggagccag	ggcagatgtt	gcattccttt	gtgtccctgt	aaatgtggga	ctacaagaag	120
aggagctgcc	tgagtgggtac	tttctcttcc	tggtaatcct	ctggcccagc	ctcatggcag	180
aatagaggta	tttttaggct	atttttgtaa	tatggcttct	ggtcaaaatc	cctgtgtagc	240
tgaattccca	agccctgcat	tgtacagccc	cccactcccc	tcaccaccta	ataaaggaat	300
agttaacact	caaaaaaaaa	aaaaaacctg	ccggggcggc	cgctcgaaag	ccgaattcca	360
gcacactggc						370

<210> 141

<211> 371

<212> DNA

<213> Homo sapien

<400> 141

tagcgtgggtc	gcggccgagg	tcctctgtgc	tgctgtcac	agcccgatgg	taccagcgca	60
gggtgtaggc	agtgcaggag	ccctcatcca	gtggcaggga	acaggggtca	tcactatccc	120

aaggagcttc	aggggtcctgg	tactcctcca	cagaatactc	ggagtattca	gagtactcat	180
catcctcagg	gggtaccgc	tcttcctcct	ctgcatgaga	gacgcggagc	acaggcacag	240
catggagctg	ggagccggca	gtgtctgcag	cataactagg	gaggggtcgt	gatccagatg	300
cgatgaactg	gccctggcag	gcacagtgc	gactcatctc	ttggcgacct	gcccgggcgg	360
ccgctcgaag	c					371

<210> 142

<211> 343

<212> DNA

<213> Homo sapien

<400> 142

gcgttttgag	gccaatggtg	taaaaggaaa	tatcttcaca	taaaaactag	atggaagcat	60
tgtcagaaac	ctctttgtga	tgtttgcttt	caactcacag	agttgaacat	tccttttcat	120
agagcagttt	tgaaacactc	ttttgtagaa	tttgcaagcg	gatgattgga	tcgctatgag	180
gtcttcattg	gaaacgggat	acctttacat	aaaaactaga	cagtagcatt	ctcagaaatt	240
tctttgggat	gtgggcattc	aaccacaga	ggagaacttc	atttgataga	gcagttttga	300
aacacccttt	ttgtagaatc	tacagggtgga	catttagagt	gct		343

<210> 143

<211> 354

<212> DNA

<213> Homo sapien

<400> 143

aggtctgatg	gcagaaaaac	tcagactgtc	tgcaacttta	cagatgggtgc	attggttcag	60
catcaggagt	gggatgggaa	ggaaagcaca	ataacaagaa	aattgaaaga	tgggaaatta	120
gtgggtggagt	gtgtcatgaa	caatgtcacc	tgtactcgga	tctatgaaaa	agtagaataa	180
aaattccatc	atcactttgg	acaggagtta	attaagagaa	tgaccaagct	cagttcaatg	240
agcaaacttc	catactgttt	ctttcttttt	tttttcatta	ctgtgttcaa	ttatctttat	300
cataaacatt	ttacatgcag	ctatttcaaa	gtgtgttgga	ttaattagga	tcat	354

<210> 144

<211> 353

<212> DNA

<213> Homo sapien

<400> 144

ggtcaaggac	ctggggggacc	cccagggtcca	gcagccacat	gattctgcag	cagacagggga	60
cctagagcac	atctggatct	cagccccacc	cctggcaacc	tgcttgccct	gagaactccc	120
aagatgacag	actaagtagg	attctgccat	ttagaataat	tctggtatcc	tgggcggttg	180
gttaagttgc	ttaaactttca	ttctgtctta	cgatagtctt	cagaggtggg	aacagatgaa	240
gaaaccatgc	cccagagaag	gttaagtgc	ttcctcttta	tggagccagt	gttccaacct	300
aggtttgcct	gataccagac	ctgtggcccc	acctcccatg	caggtctctg	tgg	353

<210> 145

<211> 371

<212> DNA

<213> Homo sapien

<400> 145

caggtctgtc	ataaactggg	ctggagtttc	tgacgactcc	ttgttcacca	aatgcaccat	60
ttcctgagac	ttgctggcct	ctccgttgag	tccacttggc	tttctgtcct	ccacagctcc	120
attgccactg	ttgatcacta	gctttttctt	ctgcccacac	cttcttcgac	tgttgactgc	180
aatgcaaact	gcaagaatca	aagccaaggc	caagagggat	gccaaagatga	tcagccattc	240

```

tggaatttgg ggtgtcctta taggaccaga ggttgtgttt gctccacctt cttgactccc 300
atgtgagacc tcggccgcga ccacgctaag ccgaattcca gcacactggc ggcccgttac 360
tagtggatcc g 371

```

```

<210> 146
<211> 355
<212> DNA
<213> Homo sapien

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```

<400> 146
ggtcctccgt cctcttccca gaggtgtcgg ggcttggccc cagcctccat cttcgtctct 60
caggatggcg agtagcagcg gctccaaggc tgaattcatt gtcggaggga aatataaaact 120
ggtacggaag atcgggtctg gtccttcggg ggacatctat ttggcgatca acatcaccaa 180
cggcgaggaa gtggcagtga agctagaatc tcagaaggcc aggcaccccc agttgctgta 240
cgagagcaag ctctataaga ttcttcaagg tgggggttggc atccccaca tacggtggta 300
tggtcaggaa aaagactaca atgtactagt catggatctt ctgggaccta gcctc 355

```

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<210> 147
<211> 355
<212> DNA
<213> Homo sapien

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```

<400> 147
ggtctgttac aaaatgaaga cagacaacac aacatttact ctgtggagat atcctactca 60
tactatgcac gtgctgtgat tttgaacata actcgtccca aaaacttgtc acgatcatcc 120
tgacttttta gggtggctga tccatcaatc ttgcactcaa ctgttacttc tttcccagtg 180
ttgttaggag caaagctgac ctgaacagca accaatggct gtagataccc aacatgcagt 240
tttttcccat aatatgggaa atattttaag tctatcatte cattatgagg ataaactgct 300
acatttggtg tatcttcatt ctttgaaaca caatctatcc ttggcactcc ttcag 355

```

```

<210> 148
<211> 369
<212> DNA
<213> Homo sapien

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```

<400> 148
aggtctctct cccctctccc ctctcctgcc agccaagtga agacatgctt acttcccctt 60
caccttccct catgatgtgg gaagagtgtc gcaaccagc cctagccaac accgcatgag 120
agggagtgtg ccgagggtct ctgagaaggc ttctctcaca tctagaaaga agcgcttaag 180
atgtggcagc ccctcttctt caagtggctc ttgtcctgtt gccctgggag ttctcaaatt 240
gctgcagcag cctccatcca gcctgaggat gacatcaata cacagaggaa gaagagtcag 300
gaaaagatga gagaagttac agactctcct gggcgacccc gagagcttac cattcctcag 360
acttcttca 369

```

```

<210> 149
<211> 620
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1) ... (620)
<223> n = A,T,C or G

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```

<400> 149

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actagtcaaa	aatgctaaaa	taatttggga	gaaaatattt	tttaagtagt	gttatagttt	60
catgtttatc	ttttattatg	ttttgtgaag	ttgtgtcttt	tcactaatta	cctatactat	120
gccaatattt	ccttatatct	atccataaca	tttatactac	atttgtaana	naatatgcac	180
gtgaaactta	acactttata	aggtaaaaat	gaggtttcca	anatttaata	atctgatcaa	240
gttcttggtta	tttccaaata	gaatggactt	ggtctgttaa	gggctaagga	gaagaggaag	300
ataagggttaa	aagttgttaa	tgaccaaaca	ttctaaaaga	aatgcaaaaa	aaaagtttat	360
tttcaagcct	tcgaactatt	taaggaaaagc	aaaatcattt	cctaaatgca	tatcatttgt	420
gagaatttct	cattaatatc	ctgaatcatt	catttcacta	aggctcatgt	tnactccgat	480
atgtctctaa	gaaagtacta	tttcatgggc	caaacctggt	tgccatantt	gggtaaaggc	540
tttcccttaa	gtgtgaaant	atttaaaatg	aaattttcct	ctttttaaaa	attctttana	600
aggggttaagg	gtgttgggga					620

<210> 150

<211> 371

<212> DNA

<213> Homo sapien

<400> 150

gggtccgatca	aaacctgcta	cctccccaag	actttactag	tgccgataaa	ctttctcaaa	60
gagcaaccag	tatcacttcc	ctgtttataa	aacctctaac	catctctttg	ttctttgaac	120
atgctgaaaa	ccacctgggc	tgcatgtatg	ccgaatttg	yaattctttt	ctctcaaagt	180
aaaatttaat	tttagggatt	catttctata	ttttcacata	tgtagtatta	ttatttcctt	240
atatgtgtaa	ggtgaaattt	atggtatttg	agtgtgcaag	aaaatatatt	tttaaagctt	300
tcatttttcc	cccagtgaat	gatttagaat	tttttatgta	aataacaga	atgttttttc	360
ttacttttat	a					371

<210> 151

<211> 4655

<212> DNA

<213> Homo sapien

<400> 151

gggacttgag	ttctgttatt	ttcttaagta	gattcatatt	gtaagggtct	cggggtgggg	60
gggttggcaa	aatcctggag	ccagaagaaa	ggacagcagc	attgatcaat	cttacagcta	120
acatgttgta	cctggaaaac	aatgccaga	ctcaatttag	tgagccacag	tacacgaacc	180
tggggctcct	gaacagcatg	gaccagcaga	ttcagaacgg	ctcctcgctc	accagtcctt	240
ataacacaga	ccacgcgcag	aacagcgtca	cggcgccctc	gccctacgca	cagcccagct	300
ccaccttcga	tgctctctct	ccatcacccg	ccatcccttc	caacaccgac	taccagggcc	360
cgcacagttt	cgacgtgtcc	ttccagcagt	cgagcaccgc	caagtcggcc	acctggacgt	420
attccactga	actgaagaaa	ctctactgcc	aaattgcaaa	gacatgcccc	atccagatca	480
aggtgatgac	cccacctcct	cagggagctg	ttatccgcgc	catgcctgtc	tacaaaaaag	540
ctgagcacgt	cacggagggtg	gtgaagcggg	gccccaacca	tgagctgagc	cgtgaattca	600
acgagggaca	gattgccccct	yctagtcatt	tgattcgagt	agaggggaac	agccatgccc	660
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cggatgaaga	tagcatcaga	aagcagcaag	tttcggacag	tacaaagaac	ggtgatggta	960
cgaagcgccc	gtttcgtcag	aacacacatg	gtatccagat	gacatccatc	aagaaacgaa	1020
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tggatgaagat	caaagagtcc	ctggaactca	tgacgtacct	tcttcagcac	acaattgaaa	1140
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gagacatgaa	tggactcagc	cccacccagg	cactccctcc	cccactctcc	atgccatcca	1440
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tgcagagatt	tctcattgac	ttttataaag	catgttcacc	cttatagtct	aagactatat	2220
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aatgtaattt	aaatgaaaga	aaattgagtt	gcacttattg	accatttttt	aattttactg	2340
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ccagttcaaa	aacacccgac	gtcatgtatt	tgagcatatc	agtaaccccc	ttaaatttaa	2760
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gaattctgat	tgattttgatt	gggatgaatg	ccatctatct	agttctaaca	gtgaagtttt	2940
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aatattgttt	ggtaaatggt	tcttttgttt	ggtaaatggt	tcytttaaag	accctcctat	3120
tctataaaac	tctgcatgta	gaggcttggt	tacctttctc	tctctaagggt	ttacaatagg	3180
agtgggtgatt	tgaaaaatat	aaaattatga	gattgggttt	cctgtggcat	aaattgcac	3240
actgtatcat	tttctttttt	aaccggtaag	agtttcagtt	tggttgaaaag	taactgtgag	3300
aaccagttt	cccgctccatc	tcctttaggg	actaccata	gacatgaaag	gtccccacg	3360
agcaagagat	aagtctttca	tggtctgtgt	tgcttaaacc	acttaaacga	agagtctcct	3420
tgaaactttg	ggaaaacatg	ttaatgacaa	tattccagat	ctttcagaaa	tataacacat	3480
ttttttgcat	gcatgcaaat	gagctctgaa	atcttcccat	gcattctggg	caagggtgt	3540
cattgcacat	aagcttccat	tttaatttta	aagtgcataa	gggccagcgt	ggctctaaaa	3600
ggtaaatgtg	ggattgcctc	tgaaaagtgt	gtatatattt	tgtgtgaaat	tgcatacttt	3660
gtattttgat	tatttttttt	ttcttcttgg	gatagtggga	tttccagaac	cacacttgaa	3720
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<210> 152
 <211> 586
 <212> PRT
 <213> Homo sapien

<400> 152
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 20 25 30
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
 35 40 45
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
 50 55 60
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65 70 75 80
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
 85 90 95
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
 100 105 110
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
 115 120 125
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
 130 135 140
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
 145 150 155 160
 Glu Gly Gln Ile Ala Pro Ser Ser His Leu Ile Arg Val Glu Gly Asn
 165 170 175
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val
 180 185 190
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val
 195 200 205
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg
 210 215 220
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val
 225 230 235 240
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg
 245 250 255
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp
 260 265 270
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr
 275 280 285
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp
 290 295 300
 Glu Leu Val Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu
 305 310 315 320
 Val Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Leu Gln His
 325 330 335
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln Gln His Gln His Leu
 340 345 350
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser
 355 360 365
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val
 370 375 380

Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr
 385 390 395 400
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met
 405 410 415
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro
 420 425 430
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro
 435 440 445
 Tyr Pro Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys
 450 455 460
 Ser Ser Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr
 465 470 475 480
 Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro
 485 490 495
 Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln
 500 505 510
 Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser
 515 520 525
 Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val
 530 535 540
 Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro
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 Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu
 580 585

<210> 153
 <211> 2007
 <212> DNA
 <213> Homo sapien

<400> 153
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 acttctggga ccctctcaac caagataagg aagtgtgtcg ggggaagctg gtggcagact 360
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 tgacggatgg caagctggag gtgccgcact ttgacagcaa gggcgagggtg gaggagtact 480
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 aaaatgagaa gcctcggaac ttggagcttc tctcctacca ctaatgggag ggcagattat 1260
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catttatcca	ttctgcaaac	ttttcttgag	caccagcacg	gggtggccatt	tgtggacttc	1620
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<210> 154

<211> 2148

<212> DNA

<213> Homo sapien

<400> 154

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<210> 155
 <211> 153
 <212> PRT
 <213> Homo sapien

<400> 155
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 Trp Arg Pro Val Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val
 20 25 30
 Pro Met Gly Asp Val Pro Met Asp Gly Ile Ser Val Ala Asp Ile Gly
 35 40 45
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys
 50 55 60
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp
 65 70 75 80
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Ile Thr
 85 90 95
 Pro Glu Ala Phe Glu Lys Leu Gly Phe Pro Ala Ala Lys Glu Ile Ala
 100 105 110
 Asn Met Cys Arg Phe Tyr Glu Met Lys Pro Asp Arg Asp Val Asn Leu
 115 120 125
 Thr His Gln Leu Asn Pro Lys Val Lys Ser Phe Ser Gln Phe Ile Ser
 130 135 140
 Glu Asn Gln Gly Ala Phe Lys Gly Met
 145 150

<210> 156
 <211> 128
 <212> PRT
 <213> Homo sapien

<400> 156
 Met Thr Ser Val Arg Val Ala Ala Tyr Phe Glu Asn Phe Leu Ala Ala
 1 5 10 15
 Trp Arg Pro Val Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val
 20 25 30
 Pro Met Gly Asp Val Pro Met Asp Gly Ile Ser Val Ala Asp Ile Gly
 35 40 45
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys
 50 55 60
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp
 65 70 75 80
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Thr Ile
 85 90 95
 Cys Ala Ile Asp Asp Gln Lys Thr Val Glu Glu Gly Phe Met Glu Asp
 100 105 110
 Val Gly Leu Ser Trp Ser Leu Arg Glu His Asp His Val Ala Gly Ala
 115 120 125

<210> 157
 <211> 424
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (424)
 <223> n = A,T,C or G

<400> 157
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 aattcagtc caactgttat attaccttct ccaggaaccc tccagtgggg aaggctgcga 180
 tattagattt ccttgatgac aaagtttttg ttgaaagctg tgctcagagg aggtgagagg 240
 agaggaagga gaaaactgca tcataacttt acagaattga atctagagtc ttccccgaaa 300
 agcccagaaa cttctctgcn gnatctggct tgtccatctg gtctaagggt gctgcttctt 360
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 tgct 424

<210> 158
 <211> 2099
 <212> DNA
 <213> Homo sapien

<400> 158
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 ccgcgcagag cccgcgccag ggccgcgcgc cgcagagcag ttaaaacgtg caggcaccag 180
 aaggcacttc ctgtcgggtga agaagacctg tctccggtgt cacgggcatc ctgtgttttg 240
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 attgacattc gtatcatcac tgtgcacatc tggcttctag gcactccagt ggggtaggag 480
 aaggaggctc gaaacctctg cagagggatc ttgccctcat tctttgggtc tgaaacactg 540
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 atctttatct tccgagtcac gatcctcgtg gtggctgccc aggaagtgtg ggggtgacgag 720
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 cgaggagaga agaggaatga tttcaaagac atagaggaca ttaaaaagca gaaggttcgg 960
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 tacgcttaag gtggaaagtg ttcattgcac aatatatttt tactgctttc tgaatgtaga 1980

cggaacagtg tggaagcaga aggcctttttt aactcatccg tttgccaatc attgcaaaca 2040
actgaaatgt ggatgtgatt gcctcaataa agctcgtccc cattgcttaa aaaaaaaaaa 2099

<210> 159
<211> 291
<212> PRT
<213> Homo sapien

<400> 159
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35 40 45
Glu Asp Phe Val Cys Asn Thr Leu Gln Pro Gly Cys Lys Asn Val Cys
50 55 60
Tyr Asp His Phe Phe Pro Val Ser His Ile Arg Leu Trp Ala Leu Gln
65 70 75 80
Leu Ile Phe Val Ser Thr Pro Ala Leu Leu Val Ala Met His Val Ala
85 90 95
Tyr Tyr Arg His Glu Thr Thr Arg Lys Phe Arg Arg Gly Glu Lys Arg
100 105 110
Asn Asp Phe Lys Asp Ile Glu Asp Ile Lys Lys Gln Lys Val Arg Ile
115 120 125
Glu Gly Ser Leu Trp Trp Thr Tyr Thr Ser Ser Ile Phe Phe Arg Ile
130 135 140
Ile Phe Glu Ala Ala Phe Met Tyr Val Phe Tyr Phe Leu Tyr Asn Gly
145 150 155 160
Tyr His Leu Pro Trp Val Leu Lys Cys Gly Ile Asp Pro Cys Pro Asn
165 170 175
Leu Val Asp Cys Phe Ile Ser Arg Pro Thr Glu Lys Thr Val Phe Thr
180 185 190
Ile Phe Met Ile Ser Ala Ser Val Ile Cys Met Leu Leu Asn Val Ala
195 200 205
Glu Leu Cys Tyr Leu Leu Leu Lys Val Cys Phe Arg Arg Ser Lys Arg
210 215 220
Ala Gln Thr Gln Lys Asn His Pro Asn His Ala Leu Lys Glu Ser Lys
225 230 235 240
Gln Asn Glu Met Asn Glu Leu Ile Ser Asp Ser Gly Gln Asn Ala Ile
245 250 255
Thr Gly Ser Gln Ala Lys His Phe Lys Val Lys Cys Ser Cys Val Ile
260 265 270
Arg Arg Leu Leu Ser Ser Pro Glu Gly Asn Thr Asn Leu Lys Val Pro
275 280 285
Ser Val Ala
290

<210> 160
<211> 3951
<212> DNA
<213> Homo sapien

<400> 160
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tgtgactctc	ctggttgcc	taagttcaga	actcccatc	ctgggagctg	gagtacagct	180
tcaagacaat	gggtataatg	gattgctcat	tgcaattaat	cctcaggtag	ctgagaatca	240
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taccaagaga	agagtatttt	tcagaaatat	aaagattttta	atacctgcca	catggaaagc	360
taataataac	agcaaaataa	aacaagaatc	atatgaaaag	gcaaagtgtca	tagtgactga	420
ctgggtatggg	gcacatggag	atgatccata	caccctacaa	tacagagggg	gtggaaaaga	480
gggaaaatac	attcattttca	cacctaat	cctactgaat	gataacttaa	cagctggcta	540
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tgagtataac	aatgacaaac	ctttctacat	aaatgggcaa	aatcaaatta	aagtgacaag	660
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ctgtattatt	agtaagcttt	ttaaagaagg	atgcaccttt	atctacaata	gcacccaaaa	780
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aagtacccac	aaccaagaag	caccaaacct	acagaaccag	atgtgcagcc	tcagaagtgc	900
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gctggtttca	tatctgccc	ccactgtatc	agctaaaaca	gacatcagca	tttgttcagg	1260
gcttaagaaa	ggatttgagg	tgggtgaaaa	actgaatgga	aaagcttatg	gctctgtgat	1320
gatattagtg	accagcggag	atgataagct	tcttggaat	tgcttacc	ctgtgctcag	1380
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<210> 161

<211> 943

<212> PRT

<213> Homo sapien

<400> 161

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Val Gln Leu Gln Asp Asn Gly Tyr Asn Gly Leu Leu Ile Ala Ile Asn
          35          40          45
Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met
          50          55          60
Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val
          65          70          75          80
Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn
          85          90          95
Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile
          100          105          110
Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln
          115          120          125
Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn
          130          135          140
Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg
          145          150          155          160
Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu
          165          170          175
Tyr Asn Asn Asp Lys Pro Phe Tyr Ile Asn Gly Gln Asn Gln Ile Lys
          180          185          190
Val Thr Arg Cys Ser Ser Asp Ile Thr Gly Ile Phe Val Cys Glu Lys
          195          200          205
Gly Pro Cys Pro Gln Glu Asn Cys Ile Ile Ser Lys Leu Phe Lys Glu
          210          215          220
Gly Cys Thr Phe Ile Tyr Asn Ser Thr Gln Asn Ala Thr Ala Ser Ile
          225          230          235          240
Met Phe Met Gln Ser Leu Ser Ser Val Val Glu Phe Cys Asn Ala Ser
          245          250          255
Thr His Asn Gln Glu Ala Pro Asn Leu Gln Asn Gln Met Cys Ser Leu
          260          265          270
Arg Ser Ala Trp Asp Val Ile Thr Asp Ser Ala Asp Phe His His Ser
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Phe Pro Met Asn Gly Thr Glu Leu Pro Pro Pro Pro Thr Phe Ser Leu
          290          295          300

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Val Glu Ala Gly Asp Lys Val Val Cys Leu Val Leu Asp Val Ser Ser
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 Lys Met Ala Glu Ala Asp Arg Leu Leu Gln Leu Gln Gln Ala Ala Glu
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 Phe Tyr Leu Met Gln Ile Val Glu Ile His Thr Phe Val Gly Ile Ala
 340 345 350
 Ser Phe Asp Ser Lys Gly Glu Ile Arg Ala Gln Leu His Gln Ile Asn
 355 360 365
 Ser Asn Asp Asp Arg Lys Leu Leu Val Ser Tyr Leu Pro Thr Thr Val
 370 375 380
 Ser Ala Lys Thr Asp Ile Ser Ile Cys Ser Gly Leu Lys Lys Gly Phe
 385 390 395 400
 Glu Val Val Glu Lys Leu Asn Gly Lys Ala Tyr Gly Ser Val Met Ile
 405 410 415
 Leu Val Thr Ser Gly Asp Asp Lys Leu Gly Asn Cys Leu Pro Thr
 420 425 430
 Val Leu Ser Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser
 435 440 445
 Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys
 450 455 460
 Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe
 465 470 475 480
 Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln
 485 490 495
 Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn
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 Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg
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 Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr
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 675 680 685
 Val His Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile
 690 695 700
 Pro Gly Ser His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn
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 Ile Gln Met Asn Ala Pro Arg Lys Ser Val Gly Arg Asn Glu Glu Glu
 725 730 735
 Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser Val


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<210> 164

<211> 1310

<212> DNA

<213> Homo sapien

<400> 164

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<210> 165

<211> 177

<212> PRT

<213> Homo sapien

<400> 165

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Ser Tyr Ala Val Pro Ser Cys Gly Arg Ser Val Glu Gly Leu Ser Arg
          20          25          30
Arg Leu Lys Arg Ala Val Ser Glu His Gln Leu Leu His Asp Lys Gly
          35          40          45
Lys Ser Ile Gln Asp Leu Arg Arg Arg Phe Phe Leu His His Leu Ile

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      50              55              60
Ala Glu Ile His Thr Ala Glu Ile Arg Ala Thr Ser Glu Val Ser Pro
65              70              75              80
Asn Ser Lys Pro Ser Pro Asn Thr Lys Asn His Pro Val Arg Phe Gly
      85              90              95
Ser Asp Asp Glu Gly Arg Tyr Leu Thr Gln Glu Thr Asn Lys Val Glu
      100              105              110
Thr Tyr Lys Glu Gln Pro Leu Lys Thr Pro Gly Lys Lys Lys Lys Gly
      115              120              125
Lys Pro Gly Lys Arg Lys Glu Gln Glu Lys Lys Lys Arg Arg Thr Arg
      130              135              140
Ser Ala Trp Leu Asp Ser Gly Val Thr Gly Ser Gly Leu Glu Gly Asp
145              150              155              160
His Leu Ser Asp Thr Ser Thr Thr Ser Leu Glu Leu Asp Ser Arg Arg
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His

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<210> 166
<211> 177
<212> PRT
<213> Homo sapien

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      <400> 166
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Ser Tyr Ala Val Pro Ser Cys Gly Arg Ser Val Glu Gly Leu Ser Arg
      20              25              30
Arg Leu Lys Arg Ala Val Ser Glu His Gln Leu Leu His Asp Lys Gly
      35              40              45
Lys Ser Ile Gln Asp Leu Arg Arg Arg Phe Phe Leu His His Leu Ile
50              55              60
Ala Glu Ile His Thr Ala Glu Ile Arg Ala Thr Ser Glu Val Ser Pro
65              70              75              80
Asn Ser Lys Pro Ser Pro Asn Thr Lys Asn His Pro Val Arg Phe Gly
      85              90              95
Ser Asp Asp Glu Gly Arg Tyr Leu Thr Gln Glu Thr Asn Lys Val Glu
      100              105              110
Thr Tyr Lys Glu Gln Pro Leu Lys Thr Pro Gly Lys Lys Lys Lys Gly
      115              120              125
Lys Pro Gly Lys Arg Lys Glu Gln Glu Lys Lys Lys Arg Arg Thr Arg
      130              135              140
Ser Ala Trp Leu Asp Ser Gly Val Thr Gly Ser Gly Leu Glu Gly Asp
145              150              155              160
His Leu Ser Asp Thr Ser Thr Thr Ser Leu Glu Leu Asp Ser Arg Arg
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<210> 167
<211> 3362
<212> DNA
<213> Homo sapien

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<400> 167

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<210> 168
 <211> 2784
 <212> DNA
 <213> Homo sapien

<400> 168

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2784

<210> 169

<211> 592

<212> PRT

<213> Homo sapien

<400> 169

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Val	Gln	Leu	Gln	Asp	Asn	Gly	Tyr	Asn	Gly	Leu	Leu	Ile	Ala	Ile	Asn
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Pro	Gln	Val	Pro	Glu	Asn	Gln	Asn	Leu	Ile	Ser	Asn	Ile	Lys	Glu	Met
		50				55					60				
Ile	Thr	Glu	Ala	Ser	Phe	Tyr	Leu	Phe	Asn	Ala	Thr	Lys	Arg	Arg	Val
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Phe	Phe	Arg	Asn	Ile	Lys	Ile	Leu	Ile	Pro	Ala	Thr	Trp	Lys	Ala	Asn
			85						90					95	
Asn	Asn	Ser	Lys	Ile	Lys	Gln	Glu	Ser	Tyr	Glu	Lys	Ala	Asn	Val	Ile
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Val	Thr	Asp	Trp	Tyr	Gly	Ala	His	Gly	Asp	Asp	Pro	Tyr	Thr	Leu	Gln
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Tyr	Arg	Gly	Cys	Gly	Lys	Glu	Gly	Lys	Tyr	Ile	His	Phe	Thr	Pro	Asn
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Phe	Leu	Leu	Asn	Asp	Asn	Leu	Thr	Ala	Gly	Tyr	Gly	Ser	Arg	Gly	Arg
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Val	Phe	Val	His	Glu	Trp	Ala	His	Leu	Arg	Trp	Gly	Val	Phe	Asp	Glu
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Tyr	Asn	Asn	Asp	Lys	Pro	Phe	Tyr	Ile	Asn	Gly	Gln	Asn	Gln	Ile	Lys
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Val	Thr	Arg	Cys	Ser	Ser	Asp	Ile	Thr	Gly	Ile	Phe	Val	Cys	Glu	Lys
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Phe	Pro	Met	Asn	Gly	Thr	Glu	Leu	Pro	Pro	Pro	Pro	Thr	Phe	Ser	Leu
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Val	Glu	Ala	Gly	Asp	Lys	Val	Val	Cys	Leu	Val	Leu	Asp	Val	Ser	Ser
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Lys	Met	Ala	Glu	Ala	Asp	Arg	Leu	Leu	Gln	Leu	Gln	Gln	Ala	Ala	Glu
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Phe	Tyr	Leu	Met	Gln	Ile	Val	Glu	Ile	His	Thr	Phe	Val	Gly	Ile	Ala
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Ser	Phe	Asp	Ser	Lys	Gly	Glu	Ile	Arg	Ala	Gln	Leu	His	Gln	Ile	Asn
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Glu Val Val Glu Lys Leu Asn Gly Lys Ala Tyr Gly Ser Val Met Ile				400
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Leu Val Thr Ser Gly Asp Asp Lys Leu Leu Gly Asn Cys Leu Pro Thr				
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Val Leu Ser Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser				
	435		440	445
Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys				
	450		455	460
Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe				
465		470		475
Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln				480
	485		490	495
Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn				
	500		505	510
Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val				
	515		520	525
Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe Asp Pro Asp				
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Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg				
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Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr				
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<210> 170

<211> 791

<212> PRT

<213> Homo sapien

<400> 170

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Val Gln Leu Gln Asp Asn Gly Tyr Asn Gly Leu Leu Ile Ala Ile Asn				
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Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met				
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Ile Thr Glu Ala Ser Phe Tyr Leu Phe Asn Ala Thr Lys Arg Arg Val				
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Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn				
	85		90	95
Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile				
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Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln				
	115		120	125
Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn				
	130		135	140
Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg				
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Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu				

				165					170					175		
Tyr	Asn	Asn	Asp	Lys	Pro	Phe	Tyr	Ile	Asn	Gly	Gln	Asn	Gln	Ile	Lys	
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Val	Thr	Arg	Cys	Ser	Ser	Asp	Ile	Thr	Gly	Ile	Phe	Val	Cys	Glu	Lys	
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Val	Glu	Ala	Gly	Asp	Lys	Val	Val	Cys	Leu	Val	Leu	Asp	Val	Ser	Ser	
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Lys	Met	Ala	Glu	Ala	Asp	Arg	Leu	Leu	Gln	Leu	Gln	Gln	Ala	Ala	Glu	
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Phe	Tyr	Leu	Met	Gln	Ile	Val	Glu	Ile	His	Thr	Phe	Val	Gly	Ile	Ala	
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Ser	Ala	Lys	Thr	Asp	Ile	Ser	Ile	Cys	Ser	Gly	Leu	Lys	Lys	Gly	Phe	
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Glu	Val	Val	Glu	Lys	Leu	Asn	Gly	Lys	Ala	Tyr	Gly	Ser	Val	Met	Ile	
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Leu	Val	Thr	Ser	Gly	Asp	Asp	Lys	Leu	Leu	Gly	Asn	Cys	Leu	Pro	Thr	
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Phe	Phe	Val	Pro	Asp	Ile	Ser	Asn	Ser	Asn	Ser	Met	Ile	Asp	Ala	Phe	
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Ser	Arg	Ile	Ser	Ser	Gly	Thr	Gly	Asp	Ile	Phe	Gln	Gln	His	Ile	Gln	
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 660 665 670
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 <212> DNA
 <213> Homo sapien

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<211> 364
<212> PRT
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Leu Gln Ser Ser Asp His Gly Gln Thr Ser Ser Leu Trp Trp Lys Cys		
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Ser Gln Glu Gly Gly Gly Ser Gly Ser Tyr Glu Glu Gly Cys Gln Ser		
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Leu Met Glu Tyr Ala Trp Gly Arg Ala Ala Ala Met Leu Phe Cys		
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	130	135 140
Cys Gly Pro Gln Met Leu Val Phe Leu Arg Val Ile Gly Gly Leu Leu		
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Lys Tyr Thr Gln Thr Phe Thr Leu His Ala Asn Pro Ala Val Thr Tyr		
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tcagaataat	tatcacagga	acttaaatgt	taagccatta	gcatagaaaa	actgttctca	2460
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gcaaaattgt	tccttttttt	tgaaaatttt	atatacttta	taatgataga	agtccaaccg	2640
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acacagttat	tagttaaatc	aaatgttcaa	aaatacggag	cagtgcctag	tactctggaga	2820
gcagcactac	cattttattct	ttcatttata	gttgggaaaag	tttttgacgg	tactaacaaa	2880
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gttttagctac	atgattgaat	gcataataaa	tgttttgtgc	ttctgactat	caatacctaa	3000
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gcttgcttta	taggatgctt	agtttgccac	tacacttcag	accaatggga	cagtcataga	3120
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aaattagact	ccaccttaag	tagtaaagta	taacaggatt	tctgtatact	gtgcaatcag	3300
ttctttgaaa	aaaaagtcaa	aagatagaga	atacaagaaa	agttttnggg	atataatttg	3360
aatgactgtg	aaaacatatg	acctttgata	acgaactcat	ttgctcactc	cttgacagca	3420
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ccctttttgt	cactggtttc	tcctagcatt	catgattttt	ttttcacaca	atgaattaaa	3780
attgctaaaa	tcattggactg	gctttctggg	tggattttcag	gtaagatgtg	tttaaggcca	3840
gagctttttc	cagtatttga	tttttttccc	caatatattga	ttttttaaaa	atatacacat	3900
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gtatggcnaa	tcanaattta	cttttaactta	agcattttgta	atttgagta	tctgggtacta	4020
gctaagaaat	aattcnataa	ttgagttttg	tactcnccaa	anatgggtca	ttcctcatgn	4080
ataatgtnc	cccaatgcag	cttcattttc	caganacctt	gacgcaggat	aaattttttc	4140

atcatttagg tccccaaaaa aaaaaaaaaa aaaaaaaaaa a

4181

<210> 176

<211> 580

<212> PRT

<213> Homo sapiens

<400> 176

Met Asn Lys Leu Tyr Ile Gly Asn Leu Ser Glu Asn Ala Ala Pro Ser
5 10 15

Asp Leu Glu Ser Ile Phe Lys Asp Ala Lys Ile Pro Val Ser Gly Pro
20 25 30

Phe Leu Val Lys Thr Gly Tyr Ala Phe Val Asp Cys Pro Asp Glu Ser
35 40 45

Trp Ala Leu Lys Ala Ile Glu Ala Leu Ser Gly Lys Ile Glu Leu His
50 55 60

Gly Lys Pro Ile Glu Val Glu His Ser Val Pro Lys Arg Gln Arg Ile
65 70 75 80

Arg Lys Leu Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu Val
85 90 95

Leu Asp Ser Leu Leu Val Gln Tyr Gly Val Val Glu Ser Cys Glu Gln
100 105 110

Val	Asn	Thr	Asp	Ser	Glu	Thr	Ala	Val	Val	Asn	Val	Thr	Tyr	Ser	Ser
		115					120					125			

Lys Asp Gln Ala Arg Gln Ala Leu Asp Lys Leu Asn Gly Phe Gln Leu
130 135 140

Glu Asn Phe Thr Leu Lys Val Ala Tyr Ile Pro Asp Glu Met Ala Ala
145 150 155 160

Gln Gln Asn Pro Leu Gln Gln Pro Arg Gly Arg Arg Gly Leu Gly Gln
165 170 175

Arg Gly Ser Ser Arg Gln Gly Ser Pro Gly Ser Val Ser Lys Gln Lys
180 185 190

Pro Cys Asp Leu Pro Leu Arg Leu Leu Val Pro Thr Gln Phe Val Gly
195 200 205

Ala Ile Ile Gly Lys Glu Gly Ala Thr Ile Arg Asn Ile Thr Lys Gln
210 215 220

Thr Gln Ser Lys Ile Asp Val His Arg Lys Glu Asn Ala Gly Ala Ala
225 230 235 240

Glu Lys Ser Ile Thr Ile Leu Ser Thr Pro Glu Gly Thr Ser Ala Ala
245 250 255

Cys Lys Ser Ile Leu Glu Ile Met His Lys Glu Ala Gln Asp Ile Lys
 260 265 270
 Phe Thr Glu Glu Ile Pro Leu Lys Ile Leu Ala His Asn Asn Phe Val
 275 280 285
 Gly Arg Leu Ile Gly Lys Glu Gly Arg Asn Leu Lys Lys Ile Glu Gln
 290 295 300
 Asp Thr Asp Thr Lys Ile Thr Ile Ser Pro Leu Gln Glu Leu Thr Leu
 305 310 315 320
 Tyr Asn Pro Glu Arg Thr Ile Thr Val Lys Gly Asn Val Glu Thr Cys
 325 330 335
 Ala Lys Ala Glu Glu Glu Ile Met Lys Lys Ile Arg Glu Ser Tyr Glu
 340 345 350
 Asn Asp Ile Ala Ser Met Asn Leu Gln Ala His Leu Ile Pro Gly Leu
 355 360 365
 Asn Leu Asn Ala Leu Gly Leu Phe Pro Pro Thr Ser Gly Met Pro Pro
 370 375 380
 Pro Thr Ser Gly Pro Pro Ser Ala Met Thr Pro Pro Tyr Pro Gln Phe
 385 390 395 400
 Glu Gln Ser Glu Thr Glu Thr Val His Gln Phe Ile Pro Ala Leu Ser
 405 410 415
 Val Gly Ala Ile Ile Gly Lys Gln Gly Gln His Ile Lys Gln Leu Ser
 420 425 430
 Arg Phe Ala Gly Ala Ser Ile Lys Ile Ala Pro Ala Glu Ala Pro Asp
 435 440 445
 Ala Lys Val Arg Met Val Ile Ile Thr Gly Pro Pro Glu Ala Gln Phe
 450 455 460
 Lys Ala Gln Gly Arg Ile Tyr Gly Lys Ile Lys Glu Glu Asn Phe Val
 465 470 475 480
 Ser Pro Lys Glu Glu Val Lys Leu Glu Ala His Ile Arg Val Pro Ser
 485 490 495
 Phe Ala Ala Gly Arg Val Ile Gly Lys Gly Gly Lys Thr Val Asn Glu
 500 505 510
 Leu Gln Asn Leu Ser Ser Ala Glu Val Val Val Pro Arg Asp Gln Thr
 515 520 525
 Pro Asp Glu Asn Asp Gln Val Val Val Lys Ile Thr Gly His Phe Tyr
 530 535 540

Ala Cys Gln Val Ala Gln Arg Lys Ile Gln Glu Ile Leu Thr Gln Val
 545 550 555 560

Lys Gln His Gln Gln Gln Lys Ala Leu Gln Ser Gly Pro Pro Gln Ser
 565 570 575

Arg Arg Lys

<210> 177

<211> 401

<212> DNA

<213> Homo sapiens

<400> 177

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atgccccgta aatgtcttca gtgttcttca gggtagttgg gatctcaaaa gatttggttc 60
agatccaaac aaatacacat tctgtgtttt agctcagtgt tttctaaaaa aagaaactgc 120
cacacagcaa aaaattgttt actttgttgg acaaaccaaa tcagttctca aaaaatgacc 180
ggtgcttata aaaagttata aatatcgagt agctctaaaa caaaccacct gaccaagagg 240
gaagtgagct tgtgcttagt atttacattg gatgccagtt ttgtaatcac tgacttatgt 300
gcaaaactggt gcagaaattc tataaactct ttgctgtttt tgatacctgc tttttgtttc 360
attttgtttt gttttgtaaa aatgataaaa cttcagaaaa t 401
```

<210> 178

<211> 561

<212> DNA

<213> Homo sapiens

<400> 178

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acgcctttca aggggtgtacg caaagcactc attgataccc ttttggtatgg ctatgaaaca 60
gcccgcctatg ggacaggggt ctttggccag aatgagtacc tacgctatca ggaggccctg 120
agtgaagctgg ccactgcggg taaagcacga attgggagct ctcagcgaca tcaccagtca 180
gcagccaaag acctaactca gtcccttgag gtctcccaa caaccatcca ggtgacatac 240
ctccctccca gtcagaagag taaacgtgcc aagcacttcc ttgaattgaa gagctttaag 300
gataactata acacattgga gagtactctg tgacggagct gaaggactct tgccgtagat 360
taagccagtc agttgcaatg tgcaagacag gctgcttgcc gggccgcctt cggaacatct 420
ggcccagcag gccagactg tatccatcca agttcccgtt gtatccagag ttcttagagc 480
ttgtgtctaa agggtaattc cccaaccctt ccttatgagc atttttagaa cattggctaa 540
gactattttc cccagtagc g 561
```

<210> 179

<211> 521

<212> DNA

<213> Homo sapiens

<400> 179

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cccaacgcgt ttgcaaatat tcccctggta gcctacttcc ttacccccga atattggtaa 60
gatcgagcaa tggcttcagg acatgggttc tcttctcctg tgatcattca agtgctcact 120
gcatgaagac tggcttgtct cagtgtttca acctcaccag ggctgtctct tgggtccacac 180
ctcgctccct gttagtgcg tatgacagcc cccatcaa atgaccttggtc aagtcacggg 240
ttctctgtgg tcaaggttgg ttggctgatt ggtggaaagt aggggtggacc aaaggaggcc 300
acgtgagcag tcagcaccag ttctgcacca gcagcgctc cgtcctagtg ggtgttctctg 360
tttctcctgg cctgggtgg gctagggcct gattcgggaa gatgccttg cagggagggg 420
aggataagtg ggatctacca attgattctg gcaaaacaat ttctaagatt tttttgcttt 480
```


atgtgggaaa cagatctaaa tctcatttta tgctgtattt t 521

<210> 180

<211> 417

<212> DNA

<213> Homo sapiens

<400> 180

ggtggaattc gccgaagatg gcggaggtgc aggtcctggt gcttgatggt cgaggccatc 60
 tcctgggccc cctggcggcc atcgtggcta aacagggtact gctgggcccg aaggtggtgg 120
 tcgtacgctg tgaaggcatc aacatttctg gcaatttcta cagaaacaag ttgaagtacc 180
 tggctttcct cgcgaagcgg atgaacacca acccttcccc aggccctac cacttccggg 240
 cccccagccg catcttcttg cggaccgtgc gaggtatgct gcccacaaa accaagcgag 300
 gccaggccgc tctggaccgt ctcaagggtg ttgacggcat cccaccgcc tacgacaaga 360
 aaaagcggat ggtggttcct gctgccctca aggtcgtgcy tctgaagcct acaagaa 417

<210> 181

<211> 283

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (35)

<223> n=A,T,C or G

<400> 181

gattttcttct aaataggatg taaaacttct ttcanattac tcttcctcag tcttgctgc 60
 caagaactca agtgtaactg tgataaaata acctttccca ggtatattgg caggtatgtg 120
 tgtaattctca gaatacacag gtgacataga tatgatatga caactggtaa tgggtggattc 180
 atttacattg tttacacttc tatgaccagg ccttaaggga aggtcagttt tttaaaaaac 240
 caagtagtgt cttcctacct atctccagat acatgtcaaa aaa 283

<210> 182

<211> 401

<212> DNA

<213> Homo sapiens

<400> 182

atattcttgc tgcttatgca gctgacattg ttgccctccc taaagcaacc aagtagcctt 60
 tatttccac agtgaaagaa aacgctggcc tatcagttac attacaaaag gcagatttca 120
 agaggattga gtaagtagtt ggatggcttt cataaaaaca agaattcaag aagaggattc 180
 atgctttaag aaacatttct tatacattcc tcacaaatta tacctgggat aaaaactatg 240
 tagcaggcag tgtgttttcc ttccatgtct ctctgcacta cctgcagtgt gtcctctgag 300
 gctgcaagtc tgtcctatct gaattcccag cagaagcact aagaagctcc accctatcac 360
 ctagcagata aaactatggg gaaaacttaa atctgtgcat a 401

<210> 183

<211> 366

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (325)

<223> n=A,T,C or G

<400> 183

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accgtgtcca agtttttaga acccttggtta gccagaccga ggtgtcctgg tcaccgtttc 60
accatcatgc tttgatgttc cctgtctttt ctctcttctg ctctcaagag caaagggttaa 120
tttaaggaca aagatgaagt cactgtaaac taatctgtca ttgtttttac cttccttttc 180
tttttcagtg cagaaattaa aagtaagtat aaagcaccgt gattgggagt gtttttgctg 240
gtgtcggaat cactggtaaa tgttggtctga gaacaatccc tccccttgca cttgtgaaaa 300
cactttgagc gctttaagag attancctga gaaataatta aatatctttt ctcttcaaaa 360
aaaaaa 366
```

<210> 184

<211> 370

<212> DNA

<213> Homo sapiens

<400> 184

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tcttacttca aaagaaaaat aaacataaaa aataagttgc tggttcctaa caggaaaaat 60
tttaataatt gtactgagag aaactgctta cgtacacatt gcagatcaaa tatttggagt 120
taaaatgtta gtctacatag atgggtgatt gtaactttat tgccattaaa agatttcaaa 180
ttgcattcat gcttctgtgt acacataatg aaaaatgggc aaataatgaa gatctctcct 240
tcagtctgct ctgtttaatt ctgctgtctg ctcttctcta atgctgcgtc cctaattgta 300
cacagtttag tgatatctag gagtataaag ttgtcgccca tcaataaaaa tcacaaagtt 360
ggtttaaaaa 370
```

<210> 185

<211> 107

<212> DNA

<213> Homo sapiens

<400> 185

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ctcatattat tttccttttg agaaattgga aactctttct gttgctatta tattaataaa 60
gttgggtgttt attttctggt agtcaccttc cccatttaaa aaaaaaa 107
```

<210> 186

<211> 309

<212> DNA

<213> Homo sapiens

<400> 186

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gaaaggatgg ctctggttgc cacagagctg ggacttcatg ttcttctaga gagggccaca 60
agagggccac aggggtggcc gggagttgtc agctgatgcc tgctgagagg caggaattgt 120
gccagtgagt gacagtcatg agggagtgtc tcttcttggg gaggaagaa ggtagagcct 180
ttctgtctga atgaaaggcc aaggctacag tacagggcc cgcgccagcc aggggtgttaa 240
tgcccacgta gtggaggcct ctggcagatc ctgcattcca aggtcactgg actgtacgtt 300
tttatgggtt 309
```

<210> 187

<211> 477

<212> DNA

<213> Homo sapiens

<400> 187

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ttcagtccca gcaagaagcg agaattctga gatcctccag aaagtcgagc agcaccacc 60
tccaacctcg ggccagtgtc ttcaggcttt actggggacc tgcgagctgg cctaattgtg 120
```

```

tggcctgcaa gccaggccat ccctggggcgc cacagacgag ctccgagcca ggtcaggcctt 180
cggaggccac aagctcagcc tcaggcccag gcaactgattg tggcagaggg gccactaccc 240
aaggtctagc taggcccacg acctagttac ccagacagtg agaagcccct ggaaggcaga 300
aaagttggga gcatggcaga caggggaaggg aaacattttc agggaaaaga catgtatcac 360
atgtcttcag aagcaagtca ggtttcatgt aaccgagtggt cctcttgctg gtccaaaagt 420
agcccagggc tgtagcacag gcttcacagt gatttttgtgt tcagccgtga gtcacac 477

```

<210> 188

<211> 220

<212> DNA

<213> Homo sapiens

<400> 188

```

taaatatggg agatattaat attcctctta gatgaccagt gattccaatt gteccaagtt 60
ttaaataagt accctgtgag tatgagataa attagtgaca atcagaacaa gtttcagtat 120
cagatgttca agaggaagtt gctattgcat tgattttaat attgtacat aaacactgat 180
ttttttgagc attattttgt atttgttgta ctttaataacc 220

```

<210> 189

<211> 417

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (76)

<223> n=A,T,C or G

<221> unsure

<222> (77)

<223> n=A,T,C or G

<400> 189

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accatcttga cagaggatac atgctcccaa aacgtttgtt accacactta aaaatcactg 60
ccatcattaa gcatcnnttt caaaattata gccattcatg atttactttt tccagatgac 120
tatcattatt ctagtccttt gaatttgtaa ggggaaaaaa aacaaaaaca aaaacttacg 180
atgcactttt ctccagcaca tcagatttca aattgaaaat taaagacatg ctatggtaat 240
gcacttgcta gtactacaca ctttgtacaa caaaaaacag aggcaagaaa caacggaaaag 300
agaaaagcct tcctttgttg gcccttaaac tgagtcaaga tctgaaatgt agagatgatc 360
tctgacgata cctgtatggt cttattgtgt aaataaaaatt gctggtatga aatgaca 417

```

<210> 190

<211> 497

<212> DNA

<213> Homo sapiens

<400> 190

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gcactggggc gctctcccgt cccgcgggtg ttgctgctgc tgccgctgct gctgggcctg 60
aacgcaggag ctgtcattga ctggcccaca gaggagggca aggaagtatg ggattatgtg 120
acggtcgcga aggatgccta catgttcttg tggtcttatt atgccacca ctctgcaag 180
aacttctcag aactgcccct ggtcatgttg cttcaggggc gtccaggcgg ttctagcact 240
ggatttgga aactttgagga aattggggcc cttgacagtg atctcaaacc acggaaaacc 300
acctggctcc aggtgccag tctcctatct gtggataatc ccgtgggcac tgggttcagt 360
tatgtgaatg gtagtggtgc ctatgccaa gacctggcta tgggtggctc agacatgatg 420
gttctcctga agaccttctt cagttgccac aaagaattcc agacagttcc attctacatt 480
ttctcagagt cctatgg 497

```

<210> 191
 <211> 175
 <212> DNA
 <213> Homo sapiens

<400> 191
 atgttgaata ttttgcttat taactttggt tattgtcttc tccctcgatt agaataattag 60
 ctacttgagt acaaggattt gagcctgtta cattcactgc tgaatttttag gctcctggaa 120
 gatacccgagc attcaataga gaccacacaa taaatatatg tcaaataaaa aaaaa 175

<210> 192
 <211> 526
 <212> DNA
 <213> Homo sapiens

<400> 192
 agtaaacatt attatTTTTT ttatatTTGc aaaggaaaca tatctaattc ttcctataga 60
 aagaacagta ttgctgtaat tcttttctt ttcttctca tttcctctgc cccttaaaag 120
 attgaagaaa gagaaacttg tcaactcata tccacgttat ctagcaaagt acataagaat 180
 ctatcactaa gtaatgtatc cttcagaatg tggtgggtta ccagtgcacac cccatattca 240
 tcacaaaatt aaagcaagaa gtccatagta atttatttgc taatagtggg tttttaatgc 300
 tcagagtttc tgaggtcaaa ttttatcttt tcaattacaa gctctatgat cttaaataat 360
 ttacttaatg ttttttggtg ttttttctc aaattaatat tgggtgttcaa gactatatct 420
 aattcctctg atcactttga gaaacaaact tttattaaat gtaaggcact tttctatgaa 480
 ttttaaatat aaaaataaat attgttctga ttattactga aaaaaa 526

<210> 193
 <211> 553
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (290)
 <223> n=A,T,C or G
 <221> unsure
 <222> (300)
 <223> n=A,T,C or G
 <221> unsure
 <222> (411)
 <223> n=A,T,C or G
 <221> unsure
 <222> (441)
 <223> n=A,T,C or G

<400> 193
 tccattgtgg tggaattcgc tctctggtaa aggcgtgcag gtgttgggcg cggcctctga 60
 gctgggatga gccgtgctcc cgggtggaagc aaggagagcc agccggagcc atggccagta 120
 cagtggtagc agttggactg accattgctg ctgcaggatt tgcaggccgt tacgttttgc 180
 aagccatgaa gcatatggag cctcaagtaa aacaagtttt tcaaagccta ccaaaatctg 240
 ccttcagtgg tggctattat agaggtgggt ttgaacccaa aatgacaaan cgggaagcan 300
 cattaatact aggtgtaagc cctactgcca ataaagggaa aataagagat gctcatcgac 360
 gaattatgct tttaaatcat cctgacaaag gaggatctcc ttatatagca nccaaaatca 420
 atgaagctaa agatttacta naaggtcaag ctaaaaaatg aagtaaattg atgatgaatt 480

ttaagttcgt attagtttat gtatatgagt actaagtttt tataataaaa tgcctcagag 540
ctacaatttt aaa 553

<210> 194
<211> 320
<212> DNA
<213> Homo sapiens

<400> 194
cccttcccaa tccatcagta aagaccccat ctgccttgtc catgccgttt cccaacaggg 60
atgtcacttg atatgagaat ctcaaattct aatgccttat aagcattcct tcctgtgtcc 120
attaagactc tgataattgt ctcccccca taggaatttc tcccaggaaa gaaatatatc 180
cccattctcg tttcatatca gaactaccgt ccccgatatt cccttcagag agattaaaga 240
ccagaaaaaa gtgagcctct tcatctgcac ctgtaatagt ttcagttcct attttcttcc 300
attgacccat atttatacct 320

<210> 195
<211> 320
<212> DNA
<213> Homo sapiens

<220>
<221> unsure
<222> (203)
<223> n=A,T,C or G
<221> unsure
<222> (218)
<223> n=A,T,C or G

<400> 195
aagcatgacc tggggaaatg gtcagacctt gtatttgttt tttggccttg aaagtagcaa 60
gtgaccagaa tctgccatgg caacaggctt taataaaagac ccttaaaaag acactgtctc 120
aactgtgggt ttagcaccag ccagctctct gtacatttgc tagctttagt ttttctaaga 180
ctgagtaaac ttcttatttt tanaaaagggg aggctggntt gtaactttcc ttgtacttaa 240
ttgggtaaaa gtcttttcca caaaccacca tctattttgt gaactttgtt agtcattctt 300
tatttggtaa attatgaact 320

<210> 196
<211> 357
<212> DNA
<213> Homo sapiens

<220>
<221> unsure
<222> (36)
<223> n=A,T,C or G

<400> 196
atataaaaata atacgaaact ttaaaaagca ttggantgtc agtatgttga atcagtagtt 60
tcactttaac tgtaaacaaat ttcttaggac accatttggg ctagtctctg tgtaagtgtg 120
aatactacaa aaacttatct atactgttct tatgtcattt gttatattca tagatttata 180
tgatgatatg acatctggct aaaaagaaat tattgcaaaa ctaaccacta tgtacttttt 240
tataaatact gtatggacaa aaaatggcat tttttatatt aaattgttta gctctggcaa 300
aaaaaaaaaa ttttaagagc tggtactaat aaaggattat tatgactgtt aaaaaaa 357

<210> 197
 <211> 565
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (27)
 <223> n=A,T,C or G

<400> 197
 tcagctgagt accatcagga tatttanccc tttaagtgct gttttgggag tagaaaacta 60
 aagcaacaat acttcctctt gacagctttg attggaatgg ggttattaga tcattcacct 120
 tggtcctaca ctttttagga tgcttggtga acataacacc acttataatg aacatccctg 180
 gttcctatat tttgggctat gtgggtagga attgttactt gttactgcag cagcagccct 240
 agaaagtaag cccagggtt cagatctaag ttagtccaaa agctaaatga tttaaagtca 300
 agttgtaatg ctaggcataa gcactctata atacattaaa ttataggccg agcaattagg 360
 gaatgtttct gaaacattaa acttgatatt atgtcactaa aattctaaca caaacttaaa 420
 aaatgtgtct catacatatg ctgtactagg cttcatcatg catttctaaa tttgtgtatg 480
 atttgaatat atgaaagaat ttatacaaga gtgttattta aaattattaa aaataaatgt 540
 atataatttg tacctattgt aaaaa 565

<210> 198
 <211> 484
 <212> DNA
 <213> Homo sapiens

<400> 198
 tatgtaagta ttggtgtctg ctttaaaaaa ggagaccag acttcacctg tccttttttaa 60
 acatttgaga acagtgttac tctgagcagt tgggccacct tcaccttacc cgacagctga 120
 ctggttgatg tgtccattgt cgcagtttg gctgttgccc ggacaggaca ggacctccat 180
 tgggcgcagc agcagggtggc aggggtgtgg cttgaggtgg gtggcagcgt ctggtcctcc 240
 tctctggtgc tttctgagag ggtctctaaa gcagagtgtg gttggcctgg ggggaaggcag 300
 agcacgtatt tctccctct agtacctctg catttgtgag tgttccctct ggctttctga 360
 agggcagcag actcttgagt atactgcaga ggacatgctt tatcagtagg tcctgagggc 420
 tccaggggct caactgacca agtaacacag aagttggggg atgtggccta tttgggtcgg 480
 aaac 484

<210> 199
 <211> 429
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (77)
 <223> n=A,T,C or G
 <221> unsure
 <222> (88)
 <223> n=A,T,C or G
 <221> unsure
 <222> (134)
 <223> n=A,T,C or G
 <221> unsure
 <222> (151)

<223> n=A,T,C or G
 <221> unsure
 <222> (189)
 <223> n=A,T,C or G
 <221> unsure
 <222> (227)
 <223> n=A,T,C or G
 <221> unsure
 <222> (274)
 <223> n=A,T,C or G
 <221> unsure
 <222> (319)
 <223> n=A,T,C or G

<400> 199
 gcttatgttt tttgttttaa cttttgtttt ttaacattta gaatattaca ttttgtatta 60
 tacagtacct ttctcanaca ttttgtanaa ttcatttcgg cagctcacta ggatttttgc 120
 gaacattaaa aagngtgata gcgatattag ngccaatcaa atggaaaaaa ggtagtctta 180
 ataaacaana cacaacgttt ttatacaaca tacttttaaaa tattaanaaa actccttaat 240
 attgtttcct attaatgatt attctttggg caanattttc tgatgctttt gattttctct 300
 caatttagca tttgctttng gtttttttct ctatttagca ttctgttaag gcacaaaaac 360
 tatgtactgt atgggaaatg ttgtaaatat taccttttcc acatttttaa cagacaactt 420
 tgaatccaa 429

<210> 200
 <211> 279
 <212> DNA
 <213> Homo sapiens

<400> 200
 gcttttttga ggaattacag ggaagctcct ggaattgtac atggatatct ttatccctag 60
 ggggaaatca aggagctggg caccctaat tctttatgga agtgttttaa actattttta 120
 ttttattaca agtattacta gagtagtggt tctactctaa gatttcaaaa gtgcatttta 180
 aatcatatcat gttcccgctt gcaaataat tgttattttg gtggagaaaa aaatagtata 240
 ttctacataa aaaattaaag atattaacta agaaaaaaa 279

<210> 201
 <211> 569
 <212> DNA
 <213> Homo sapiens

<400> 201
 taggtcagta ttttttagaaa ctcttaatag ctcatactct tgataccaaa agcagccctg 60
 attgttaaag cacacacctg cacaagaagc agtgatgggt gcattttacat ttcttgggtg 120
 cacaaaaaaa aattctcaaa aagcaaggac ttacgctttt tgcaaagcct ttgagaagtt 180
 actggatcat aggaagctta taacaagaat ggaagattct taaataactc actttctttg 240
 gtatccagta acagtagatg ttcaaaatat gtagctgatt aataccagca ttgtgaacgc 300
 tgtacaacct tgtgggttatt actaagcaag ttactactag cttctgaaaa gtagcttcat 360
 aattaatggt atttatacac tgccctccat gacttttact ttgccctaag ctaatctcca 420
 aaatctgaaa tgctactcca atatcagaaa aaaaggggga ggtggaatta tatttctctg 480
 gattttaaga gtacagagaa tcatgcacat ctctgattag ttcatatatg tctagtgtgt 540
 aataaaagtc aaagatgaac tctcaaaaa 569

<210> 202
 <211> 501

<212> DNA

<213> Homo sapiens

<400> 202

```
attaataggc ttaataattg ttggcaagga tccttttgct ttctttggca tgcaagctcc 60
tagcatctgg cagtggggcc aagaaaataa ggtttatgca tgtatgatgg ttttcttctt 120
gagcaacatg attgagaacc agtgtatgtc aacagggtgca tttgagataa ctttaaataga 180
tgtacctgtg tgggtctaagc tggaatctgg tcaccttcca tccatgcaac aacttggtca 240
aattcttgac aatgaaatga agctcaatgt gcatatggat tcaatcccac accatcgatc 300
atagcaccac ctatcagcac tgaaaactct tttgcattaa gggatcattg caagagcagc 360
gtgactgaca ttatgaaggc ctgtactgaa gacagcaagc tgtagtaca gaccagatgc 420
tttcttggca ggctcgttgt acctcttggg aaacctcaat gcaagatagt gtttcagatgc 480
tggcatattt tggaattctg c 501
```

<210> 203

<211> 261

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (36)

<223> n=A,T,C or G

<221> unsure

<222> (96)

<223> n=A,T,C or G

<400> 203

```
gacaagctcc tggctcttgag atgtcttctc gttaangaga tgggcctttt ggaggtaaag 60
gataaaatga atgagttctg tcatgattca ctattntata acttgcata cctttactgt 120
gttagctctt tgaatgttct tgaaatttta gactttcttt gtaaacaat gatatgtcct 180
tatcattgta taaaagctgt tatgtgcaac agtgtggaga ttccttgtct gatttaataa 240
aataacttaaa cactgaaaaa a 261
```

<210> 204

<211> 421

<212> DNA

<213> Homo sapiens

<400> 204

```
agcatctttt ctacaacgtt aaaattgcag aagtagctta tcattaataaa acaacaacaa 60
caacaataac aataaatcct aagtgtaaat cagttattct accccctacc aaggatatca 120
gcctgttttt tccctttttt ctcttgggaa taattgtggg cttcttccca aatttctaca 180
gcctctttcc tcttctcatg cttgagcttc cctgtttgca cgcattgctg tgcaggactg 240
gcttgtgtgc ttggactcgg ctccagggtg aagcatgctt tcccttggtta ctgttggaga 300
aactcaaac ttcaagccct aggtgtagcc attttgtcaa gtcattcaact gtatttttgc 360
actggcatta acaaaaaaag aagataaaat attgtacat taaacttta taaaacttta 420
a 421
```

<210> 205

<211> 460

<212> DNA

<213> Homo sapiens

<400> 205


```

tactctcaca atgaaggacc tggaatgaaa aatctgtgtc taaacaagtc ctcttttagat 60
tttagtgcaa atccagagacc agcgtcgggt gcctcgagta attctttcat gggtagcctt 120
ggaaaagctc tcaggagacc tcacctagat gcctattcaa gctttggaca gccatcagat 180
tgtcagccaa gagcctttta ttgaaaagct cattcttccc cagacttgga ctctgggtca 240
gaggaagatg ggaaagaaaag gacagatttt caggaagaaa atcacatttg tacctttaa 300
cagacttttag aaaactacag gactccaaat ttctagttt atgacttgga cacatagact 360
gaatgagacc aaaggaaaag cttaacatac tacctcaagg tgaactttta tttaaaagag 420
agagaatctt atgtttttta aatggagtta tgaattttta 460

```

<210> 206

<211> 481

<212> DNA

<213> Homo sapiens

<400> 206

```

tgtggtggaa ttcgggacgc cccagacccc tgactttttc ctgcgtgggc cgtctcctcc 60
tgcggaagca gtgacctctg acccctggtg accttcgctt tgagtgcctt ttgaacgctg 120
gtcccgcggg acttggtttt ctcaagctct gtctgtccaa agacgctccg gtcgaggtcc 180
cgctgcccct ggggtggatac ttgaacccca gacgcccctc tgtgctgctg tgcggagg 240
cggccttccc atctgcctgc ccaccggag ctctttccgc cggcgagggg tcccaagccc 300
acctcccgcc ctgactcctg cgggtgtgct ctgggcacgt cctgcacaca caatgcaagt 360
cctggcctcc gcgcccgcgc gccacgcga gccgtaccgc ccgccaactc tgttatttat 420
ggtgtgaccc cctggagggtg cctcggcccc accggggcta tttattgttt aatttatttg 480
t 481

```

<210> 207

<211> 605

<212> DNA

<213> Homo sapiens

<400> 207

```

accctttttg gattcagggc tcctcacaat taaaatgagt gtaatgaaac aagggtgaaaa 60
tatagaagca tccctttgta tactgttttg ctacttacag tgtacttggc attgctttat 120
ctcactggat tctcacggta ggatttctga gatcttaatc taagctccaa agttgtctac 180
ttttttgatc ctagggtgct ccttttgttt tacagagcag ggtcacttga tttgctagct 240
ggtggcagaa ttggcaccat taccagggtc tgactgacca ccagtcagag gcactttatt 300
tgtatcatga aatgatttga aatcatttga aagcagcgaa gtctgataat gaatgccagc 360
tttcttctgt ctttgataac aaagactcca aatattctgg agaacttggg taaaagtgtg 420
aagggtctaga ttgggatttg aagacaaaat tgtaggaaat cttacatttt tgcaataaca 480
aacattaatg aaagcaaaac attataaaaag taattttaat tcaccacata cttatcaatt 540
tcttgatgct tccaaatgac atctaccaga tatggttttg tggacatctt tttctgttta 600
cataa 605

```

<210> 208

<211> 655

<212> DNA

<213> Homo sapiens

<400> 208

```

ggcgttgttc tggattcccg tcgtaactta aagggaact ttcacaatgt ccggagccct 60
tgatgtcctg caaatgaagg agggagatgt ccttaagttc cttgcagcag gaaccactt 120
agggtggcacc aatcttgact tccagatgga acagtacatc tataaaagga aaagtgatgg 180
catctatatc ataaatctca agaggacctg ggagaagctt ctgctggcag ctctgcaat 240
tggtgccatt gaaaaccctg ctgatgtcag tgttatatcc tccaggaata ctggccagag 300
ggctgtgctg aagtttgctg ctgccactgg agccactcca attgctggcc gcttcaactc 360

```

```

tggaaccttc actaaccaga tccaggcagc cttccgggag ccacggcttc ttgtggttac 420
tgaccccagg gctgaccacc agcctctcac ggaggcatct tatgttaacc tacctaccat 480
tgcgctgtgt aacacagatt ctectctgcg ctatgtggac attgccatcc catgcaacaa 540
caagggagct cactcagtgg gtttgatgtg gtggatgctg gctcgggaag ttctgcgcac 600
gcgtggcacc atttcccgtg aacacccatg ggaggtcatg cctgatctgt acttc 655

```

<210> 209

<211> 621

<212> DNA

<213> Homo sapiens

<400> 209

```

catttagaac atggttatca tccaagacta ctctaccctg caacattgaa ctcccaagag 60
caaatccaca ttctcttga gttctgcagc ttctgtgtaa atagggcagc tgctgtctat 120
gccgtagaat cacatgatct gaggaccatt catggaagct gctaaatagc ctagtctggg 180
gagtcctcca taaagttttg catggagcaa acaaacagga ttaactagg tttggttctt 240
tcagccctct aaaagcatag ggcttagcct gcaggcttcc ttgggctttc tctgtgtgtg 300
tagttttgta aacactatag catctgttaa gatccagtgt ccatggaaac cttcccat 360
gccgtgactc tggactatat cagtttttgg aaagcagggt tcctctgcct gctaacaagc 420
ccacgtggac cagtctgaat gtctttcctt tacacctatg tttttaaata gtcaaacttc 480
aagaaacaat ctaaacaagt ttctgttgca tatgtgtttg tgaacttgta tttgtattta 540
gtaggcttct atattgcatt taacttgttt ttgtaactcc tgattcttcc ttttcggata 600
ctattgatga ataaagaaat t 621

```

<210> 210

<211> 533

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (20)

<223> n=A,T,C or G

<221> unsure

<222> (21)

<223> n=A,T,C or G

<221> unsure

<222> (61)

<223> n=A,T,C or G

<400> 210

```

cgccttgggg agccggcggn ngagtccggg acgtggagac ccgggggtccc ggcagccggg 60
nggcccgcgg gccaggggtg gggatgcacc gccgcggggt gggagctggc gccatcgcca 120
agaagaaact tgcagaggcc aagtataagg agcgaggagc ggtcttggct gaggaccagc 180
tagcccagat gtcaaagcag ttggacatgt tcaagaccaa cctggaggaa tttgccagca 240
aacacaagca ggagatccgg aagaatcctg agttccgtgt gcagttccag gacatgtgtg 300
caaccattgg cgtggatccg ctggcctctg gaaaaggatt ttggtctgag atgctgggcg 360
tgggggactt ctattacgaa ctaggtgtcc aaattatcga agtgtgcctg gcgctgaagc 420
atcggaatgg aggtctgata actttggagg aactacatca acaggtgttg aagggaagg 480
gcaagttcgc ccaggatgtc agtcaagatg acctgatcag agccatcaag aaa 533

```

<210> 211

<211> 451

<212> DNA

<213> Homo sapiens

<400> 211
 ttagcttgag ccgagaacga ggcgagaaaag ctggagaccg aggagaccgc ctagagcgga 60
 gtgaacgggg aggggaccgt ggggaccggc ttgatcgtgc gcggacacct gctaccaagc 120
 ggagcttcag caaggaagtg gaggagcgga gtagagaacg gccctcccag cctgaggggc 180
 tgcgcaaggc agctagcctc acggaggatc gggaccgtgg gcgggatgcc gtgaagcgag 240
 aagctgccct acccccagtg agccccctga aggcggctct ctctgaggag gagttagaga 300
 agaaatccaa ggctatcatt gaggaatata tccatctcaa tgacatgaaa gaggcagtcc 360
 agtgcgtgca ggagctggcc tcaccctcct tgcctctcat ctttgtacgg catggtgtcg 420
 agtctacgct ggagcgcgagt gccattgctc g 451

<210> 212
 <211> 471
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (54)
 <223> n=A,T,C or G

<400> 212
 gtgattattc ttgatcaggg agaagatcat ttagatttgt tttgcattcc ttanaatgga 60
 gggcaacatt ccacagctgc cctggctgtg atgagtgtcc ttgcaggggc cggagtagga 120
 gcaactggggg gggggcgga ttgggggttac tcgatgtaag ggattccttg ttgttgtgtt 180
 gagatccagt gcagttgtga tttctgtgga tcccagcttg gttccaggaa ttttgtgtga 240
 ttggcttaaa tccagttttc aatcttcgac agctgggctg gaacgtgaac tcagtagctg 300
 aacctgtctg acccggtcac gttcttggtat cctcagaact ctttgcctct gtcgggggtgg 360
 ggggtgggaac tcacgtgggg agcgggtggc gagaaaatgt aaggattctg gaatacatat 420
 tccatgggac tttccttccc tctcctgctt cctcttttcc tgcctccctaa c 471

<210> 213
 <211> 511
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (27)
 <223> n=A,T,C or G
 <221> unsure
 <222> (63)
 <223> n=A,T,C or G
 <221> unsure
 <222> (337)
 <223> n=A,T,C or G
 <221> unsure
 <222> (442)
 <223> n=A,T,C or G

<400> 213
 ctaattagaa acttgctgta cttttntttt tcttttaggg gtcaaggacc ctctttatag 60
 ctncatttg cctacaataa attattgcag cagtttgcaa tactaaaata ttttttatag 120
 actttatatt tttccttttg ataaagggat gctgcatagt agagttggtg taattaaact 180
 atctcagccg tttccctgct ttccttctg ctccatatgc ctcatgtcc ttccaggag 240

```

ctctttttaat cttaaagttc tacatttcat gctcttagtc aaattctggt accttttttaa 300
taactcttcc cactgcatat ttccatcttg aattggnggt tctaaattct gaaactgtag 360
ttgagataca gctattttaat atttctggga gatgtgcac cctcttcttt gtggttgccc 420
aagggttgttt tgcgtaactg anactccttg atatgcttca gagaatttag gcaaactg 480
gccatggccg tgggagtact gggagtaaaa t 511

```

<210> 214

<211> 521

<212> DNA

<213> Homo sapiens

<400> 214

```

agcattgccca aataatccct aattttccac taaaaatata atgaaatgat gttaagcttt 60
ttgaaaagtt taggttaaac ctactgttgt tagattaatg tatttggtgc ttccctttat 120
ctggaatgtg gcattagctt ttttatttta accctcttta attcttattc aattccatga 180
cttaagggtg gagagctaaa cactgggatt ttgggataac agactgacag ttttgcataa 240
ttataatcgg cattgtacat agaaaggata tggctacctt ttgttaaata tgcactttct 300
aaatatcaaa aaagggaaat gaagtataaa tcaatttttg tataatctgt ttgaaacatg 360
agtttttatt gcttaataatt agggctttgc ccttttctg taagtctctt gggatcctgt 420
gtagaagctg ttctcattaa acaccaaaca gttaagtcca ttctctggta ctagctacaa 480
attcgggttc atattctact taacaattta aataaactga a 521

```

<210> 215

<211> 381

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (17)

<223> n=A,T,C or G

<221> unsure

<222> (20)

<223> n=A,T,C or G

<221> unsure

<222> (60)

<223> n=A,T,C or G

<221> unsure

<222> (61)

<223> n=A,T,C or G

<221> unsure

<222> (365)

<223> n=A,T,C or G

<400> 215

```

gagcggagag cggaccngtn agagccctga gcagccccac cgccgcccgc ggcctagttn 60
ncatcacacc ccgggaggag ccgcagctgc cgcagccggc cccagtcacc atcacgcaa 120
ccatgagcag cgaggccgag acccagcagc cgcccgccgc ccccccgcc gccccgccc 180
tcagcgccgc cgacaccaag cccggcacta cgggcagcgg cgcagggagc ggtggcccg 240
gcggcctcac atcggcgggc cctgccggcg gggacaagaa ggtcatcgca acgaaggttt 300
tgggaacagt aaaatggttc aatgtaagga acggatatgg ttcatcaac aggaatgaca 360
ccaangaaga tgtatttgta c 381

```

<210> 216

<211> 425

<212> DNA

<213> Homo sapiens

<400> 216

```
ttactaacta ggtcattcaa ggaagtcaag ttaacttaaa catgtcacct aaatgcactt 60
gatgggtgttg aaatgtccac cttcttaaat ttttaagatg aacttagttc taaagaagat 120
aacaggccaa tcctgaagggt actccctgtt tgctgcagaa tgtcagatat tttggatgtt 180
gcataagagt cctatttgcc ccagttaatt caacttttgt ctgcctgttt tgtggactgg 240
ctggctctgt tagaactctg tccaaaaagt gcatggaata taacttgtaa agcttccac 300
aattgacaat atatatgcat gtgtttaaac caaatccaga aagcttaaac aatagagctg 360
cataatagta tttattaaag aatcacaact gtaaacaatga gaataactta aggattctag 420
tttag                                         425
```

<210> 217

<211> 181

<212> DNA

<213> Homo sapiens

<400> 217

```
gagaaaccaa atgatagggt gtagagcctg atgactccaa acaaagccat caccgcatt 60
cttctcctt cttctgggtg tacagctcca agggcccttc accttcattg ctgaaatgga 120
actttggctt tttcagtgga agaatatgtt gaaggtttca tttgttcta gaaaaaaaaa 180
a                                             181
```

<210> 218

<211> 405

<212> DNA

<213> Homo sapiens

<400> 218

```
caggccttcc agttcactga caaacatggg gaagtgtgcc cagctggctg gaaacctggc 60
agtataacca tcaagcctga tgtccaaaag agcaaagaat atttctccaa gcagaagtga 120
gcgctgggct gtttttagtg caggctgcgg tgggcagcca tgagaacaaa acctcttctg 180
tatttttttt ttccattagt aaaacacaag acttcagatt cagccgaatt gtggtgtctt 240
acaaggcagg cctttcctac aggggggtgga gagaccagcc tttcttcctt tggtaggaat 300
ggcctgagtt ggcgttgttg gcaggctact ggtttgtatg atgtattagt agagcaaccc 360
attaatcttt tgtagtttgt attaaacttg aactgagaaa aaaaaa                     405
```

<210> 219

<211> 216

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (207)

<223> n=A,T,C or G

<221> unsure

<222> (210)

<223> n=A,T,C or G

<400> 219

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actccaagag ttagggcagc agagtggagc gatttagaaa gaacatttta aaacaatcag 60
ttaatttacc atgtaaaatt gctgtaaatg ataattgtga cagattttct gttcaaatat 120
tcaattgtaa acttcttggt aagactgtta cgtttctatt gcttttgtat gggatattgc 180
```

aaaaataaaa aggaaagaac cctcttnaan aaaaaa

216

<210> 220

<211> 380

<212> DNA

<213> Homo sapiens

<400> 220

```
cttacaaatt gcccccatgt gtaggggaca cagaaccctt tgagaaaact tagatttttg 60
tctgtacaaa gtctttgcct ttttccttct tcattttttt ccagtacatt aaatttgtca 120
atttcattct tgagggaaac tgattagatg ggttggtgtt gtgttctgat ggagaaaaca 180
gcaccccaag gactcagaag atgattttta cagttcagaa cagatgtgtg caatattggt 240
gcatgtaata atgttgagtg gcagtcaaaa gtcattgatt ttatcttagt tcttcattac 300
tgcatgaaa aggaaaacct gtctgagaaa atgcctgaca gtttaattta aaactatggt 360
gtaagtcttt gacaaaaaaa                                     380
```

<210> 221

<211> 398

<212> DNA

<213> Homo sapiens

<400> 221

```
ggtttagtaag ctgtcgactt tgtaaaaaag ttaaaaatga aaaaaaaagg aaaaatgaat 60
tgtatatatta atgaatgaac atgtacaatt tgccactggg aggagggtcc tttttgttgg 120
gtgagtcctgc aagtgaattt cactgatgtt gatattcatt gtgtgtagtt ttatttcggt 180
cccagcccg tttcctttta ttttggagct aatgccagct gcgtgtctag ttttgagtgc 240
agtaaaatag aatcagcaaa tcaactctat ttttcatect tttccggtat tttttgggtt 300
gtttctgtgg gagcagtgtg caccaactct tctgtatat tgcccttttg ctggaaaatg 360
ttgtatgttg aataaaaatt tctataaaaa ttaaaaaa                                     398
```

<210> 222

<211> 301

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (49)

<223> n=A,T,C or G

<221> unsure

<222> (64)

<223> n=A,T,C or G

<400> 222

```
ttcgataatt gatctcatgg gctttccctg gaggaaggt ttttttgnt gtttattttt 60
taanaacttg aaacttgtaa actgagatgt ctgtagcttt tttgccatc tgtagtgtat 120
gtgaagattt caaaacctga gagcactttt tctttgttta gaattatgag aaaggcacta 180
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<211> 200

<212> DNA

<213> Homo sapiens

<400> 223

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<210> 224

<211> 385

<212> DNA

<213> Homo sapiens

<400> 224

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<210> 225

<211> 560

<212> PRT

<213> Homo sapien

<400> 225

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 20      25      30
Arg Pro Ser Ala Tyr Met Arg Glu His Asn Gln Leu Asn Gly Trp Ser
 35      40      45
Ser Asp Glu Asn Asp Trp Asn Glu Lys Leu Tyr Pro Val Trp Lys Arg
 50      55      60
Gly Asp Met Arg Trp Lys Asn Ser Trp Lys Gly Gly Arg Val Gln Ala
 65      70      75      80
Val Leu Thr Ser Asp Ser Pro Ala Leu Val Gly Ser Asn Ile Thr Phe
 85      90      95
Ala Val Asn Leu Ile Phe Pro Arg Cys Gln Lys Glu Asp Ala Asn Gly
100      105      110
Asn Ile Val Tyr Glu Lys Asn Cys Arg Asn Glu Ala Gly Leu Ser Ala
115      120      125
Asp Pro Tyr Val Tyr Asn Trp Thr Ala Trp Ser Glu Asp Ser Asp Gly
130      135      140
Glu Asn Gly Thr Gly Gln Ser His His Asn Val Phe Pro Asp Gly Lys
145      150      155      160
Pro Phe Pro His His Pro Gly Trp Arg Arg Trp Asn Phe Ile Tyr Val
165      170      175
Phe His Thr Leu Gly Gln Tyr Phe Gln Lys Leu Gly Arg Cys Ser Val
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Arg Val Ser Val Asn Thr Ala Asn Val Thr Leu Gly Pro Gln Leu Met
195      200      205
Glu Val Thr Val Tyr Arg Arg His Gly Arg Ala Tyr Val Pro Ile Ala

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Gln Val Lys Asp Val Tyr Val Val Thr Asp Gln Ile Pro Val Phe Val		
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	245	250
Lys Asp Leu Pro Ile Met Phe Asp Val Leu Ile His Asp Pro Ser His		255
	260	265
Phe Leu Asn Tyr Ser Thr Ile Asn Tyr Lys Trp Ser Phe Gly Asp Asn		270
	275	280
Thr Gly Leu Phe Val Ser Thr Asn His Thr Val Asn His Thr Tyr Val		285
	290	295
Leu Asn Gly Thr Phe Ser Leu Asn Leu Thr Val Lys Ala Ala Ala Pro		300
305	310	315
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Pro Asp Glu Asn Cys Gln Ile Asn Arg Tyr Gly His Phe Gln Ala Thr		350
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Ile Thr Ile Val Glu Gly Ile Leu Glu Val Asn Ile Ile Gln Met Thr		365
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Asp Val Leu Met Pro Val Pro Trp Pro Glu Ser Ser Leu Ile Asp Phe		380
385	390	395
Val Val Thr Cys Gln Gly Ser Ile Pro Thr Glu Val Cys Thr Ile Ile		400
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Ser Asp Pro Thr Cys Glu Ile Thr Gln Asn Thr Val Cys Ser Pro Val		415
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Asp Val Asp Glu Met Cys Leu Leu Thr Val Arg Arg Thr Phe Asn Gly		430
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Ser Gly Thr Tyr Cys Val Asn Leu Thr Leu Gly Asp Asp Thr Ser Leu		445
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Ala Leu Thr Ser Thr Leu Ile Ser Val Pro Asp Arg Asp Pro Ala Ser		460
465	470	475
Pro Leu Arg Met Ala Asn Ser Ala Leu Ile Ser Val Gly Cys Leu Ala		480
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Ile Phe Val Thr Val Ile Ser Leu Leu Val Tyr Lys Lys His Lys Glu		495
	500	505
Tyr Asn Pro Ile Glu Asn Ser Pro Gly Asn Val Val Arg Ser Lys Gly		510
	515	520
Leu Ser Val Phe Leu Asn Arg Ala Lys Ala Val Phe Phe Pro Gly Asn		525
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<211> 9

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<400> 229
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Phe Ser Phe Ala
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<213> Homo sapiens

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<211> 20

<212> PRT

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Asp Pro Asp Gly
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<212> PRT

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Pro Asn Ser Asp
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<212> PRT

<213> Homo sapiens

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Phe Ile Pro Pro Asn
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Gln Ile Ser Thr
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Ile Gln Asp Asp Phe
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Gln Met Asn Ala
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<212> PRT

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Ser His Ala Met
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<210> 245

<211> 20

<212> PRT

<213> Homo sapiens

<400> 245

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Pro	Glu	Ala	Phe 100	Glu	Lys	Leu	Gly	Phe 105	Pro	Ala	Ala	Lys	Glu	Ile	Ala		
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 <212> DNA
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agacaagaaa gagaatggaa caaaattatt ataatgaatt ctgcagatat ccatcacact7860
ggcggccgctcgagcaccac caccaccacc actgagatcc ggctgctaac aaagcccga7920
aggaagctgagtgtgctgct gccaccgctg agcaataact agcataaccc cttggggcct7980
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<210> 255

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 255

gtggccagng	actagaaggc	gagggcgccgc	gggaccatgg	cggcggcggc	ggacgagcgg	60
agtccanagg	acggagaaga	cgaggaagag	gaggagcagt	tggttctggt	ggaattatca	120
ggaattattg	attcagactt	cctctcaaaa	tgtgaaaata	aatgcaagg	tttgggcatt	180
gacactgaga	ggcccattct	gcaagtggac	agctgtgtct	ttgctgggga	gtatgaagac	240
actctangga	cctgtgttat	atgtgaagaa	aatgntnaac	atgctgatac	agaaggcaat	300
aataaaacag	tgctaaaata	taaatgccat	acaatgaaga	agctcagcat	gacaagaact	360
ctcctgacag	agaagaagga	aggagaagaa	aacatangtg	g		401

<210> 256

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 256

tggtggncct	gggatgggga	accgcggtgg	cttcocngga	ggtttcggca	ntggcatccg	60
gggccggggg	cgcgcccgng	gacggggccg	gggcecnangc	cgnnnganctc	gcggangcaa	120
ggccgaggat	aaggagtggg	tgcccgtcac	caacttgggc	cgcttgacca	aggacatgaa	180
nancaagccc	ctgnaggaga	tctatntctt	cttccttgcc	ccattaagga	atcaagagat	240
catttgattt	cttcctgggg	gcctctctca	aggatnaggt	ttttgaagat	tatgccagtg	300
canaaannan	accccgttgc	ccngtccatc	tncaccaaac	ncttccaagg	gnattttttg	360
tttaggcctc	attncngggg	ggaaccttaa	cccaatttgg	g		401

<210> 257

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 257

atgtatgtaa	aacacttcat	aaaatgtaaa	gggctataac	aaatatgtta	taaagtgatt	60
ctctcagccc	tgaggtatac	agaatcattt	gcctcagact	gctgttggtt	tttaaaattt	120
ttaaaatata	tgctaagtaa	tttgctatgt	cttctcccac	actatcaata	tgcttgcttc	180
taacaggctc	cccactttct	tttaatgtgc	tggtatgagc	tttggacatg	agataaccgt	240
gcctgttcag	agtgctctaca	gtaagagctg	gacaaactct	ggagggacac	agtccttgag	300
acagctcttt	tggttgcttt	ccacttttct	gaaaggttca	cagtaacctt	ctagataata	360
gaaactccca	gttaaagcct	angctancaa	ttttttttag	t		401

<210> 258

<211> 401

<212> DNA

<213> Homo sapien

<400> 258
 ggagcgctag gtcggtgtac gaccgagatt aggggtgcgtg ccagctccgg gaggccgcgg 60
 tgaggggccc ggcccaagct gccgaccga gccgatcgtc agggtcgcca gcgcctcagc 120
 tctgtggagg agcagcagta gtcggagggt gcaggatatt agaaatggct actccccagt 180
 caattttcat ctttgcaatc tgcattttta tgataacaga attaatcttg gcctcaaaaa 240
 gctactatga tatcttaggt gtgccaaaat cggcatcaga gcgccaaatc aagaaggcct 300
 ttcacaagtt ggccatgaag taccaccctg acaaaaataa gaccagatg ctgaagcaaa 360
 attcagagag attgcagaag catatgaaac actctcagat g 401

<210> 259
 <211> 401
 <212> DNA
 <213> Homo sapien

<400> 259
 attgggtttg gagggaggat gatgacagag gaatgccctt tggccatcac ggttttgatt 60
 ctccagaata ttgtgggttt gatcatcaat gcagtcattg taggctgcat tttcatgaaa 120
 acagctcagg ctcacagaag ggcagaaact ttgattttca gccgccatgc tgtgattgcc 180
 gtccgaaatg gcaagctgtg cttcatgttc cgagtgggtg acctgaggaa aagcatgac 240
 attagtgcct ctgtgcgcac ccagggtggtc aagaaaacaa ctacacctga aggggagggtg 300
 gttcctattc accaactgga cattcctgtt gataacccaa tcgagagcaa taacattttt 360
 ctggtggccc ctttgatcat ctgccacgtg attgacaagc g 401

<210> 260
 <211> 363
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (363)
 <223> n = A,T,C or G

<400> 260
 aggaganang gagggggana tgaataggga tggagaggga natagtggat gagcagggca 60
 canggagagg aancagaaag gagaggcaag acaggagagac acacancaca nangangana 120
 cagggtggggg ctgggggtggg gcatggagag ccttttnangt cncccaggcc acctgctct 180
 cgctggnctg ttgaaaccca ctccatggct tcttgccact gcagttgggc ccagggtgg 240
 cttattnctg gaatgcaagt ggctgtggct tggagcctcc cctctggnnn anggaaannn 300
 attgctccct tatctgcttg gaatatctga gtttttccan cccggaaata aaacacacac 360
 aca 363

<210> 261
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (401)
 <223> n = A,T,C or G

<400> 261
 cggctctccg ccgctctccc ggggtttcgg ggcacttggg tcccacagtc tggctctgct 60
 tcaccttccc ctgacctgag tagtcgccat ggcacaggtt ctcagaggca ctgngactga 120

```

cttccttgga tttgatgagc gggctgatgc anaaactctt cggaaggcta tgaaaggctt 180
gggcacagat gaggagagca tcctgactct gttgacatcc cgaagtaatg ctgagcgcca 240
ggaaatctct gcagctttta agactctgtt tggcagggat cttctggatg acctgaaatc 300
agaactaact ggaaaatttg aaaaattaat tgtggctctg atgaaaccct ctcggtttta 360
tgatgcttat gaactgaaac atgccttgaa gggagctgga a 401

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<210> 262

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 262

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agtctanaac atttctaata ttttgngett tcatatatca aaggagatta tgtgaaacta 60
tttttaataa ctgtaaagtg acatatagtt ataagatata tttctgtaca gtagagaaag 120
agtttataac atgaagaata ttgtaccatt atacattttc attctcgatc tcataagaaa 180
ttcaaaaagaa taatgataga ggtgaaaata tgtttacttt ctctaaatca agcctagttg 240
tcaactcaaa aattatgntg catagtttta ttttgaattt aggttttggg actacttttt 300
tccancttca atgagaaaat aaaatctaca actcaggagt tactacagaa gttctaanta 360
tttttttgct aannagcnaa aaatataaac atatgaaaat g 401

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<210> 263

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 263

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ctgtccgacc aagagaggcc ggccgagccc gaggcttggg cttttgcttt ctggcggagg 60
gatctgcggc ggtttaggag gcggcgctga tcctgggagg aagaggcagc tacggcggcg 120
gcggcggttg cggctagggc ggcggcgaat aaaggggccc ccgcccgggtg atgcggtgac 180
cactgcggca ggcccaggag ctgagtgggc cccggccctc agcccgtccc gncggacccg 240
ctttcctcaa ctctccatct tctcctgccg accgagatcg ccgaggcggn ctcaggctcc 300
ctanccctt ccccgccct tccccncccc cgccccgcc ccggggggccg ccgccacccg 360
cctcccacca tggtcttgaa ganaatccac aaggaattga a 401

```

<210> 264

<211> 401

<212> DNA

<213> Homo sapien

<400> 264

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aacaccagcc actccaggac ccctgaaggc ctctaccagg tcaccagtgt tctgcgccta 60
aagccacccc ctggcagaaa cttcagctgt gtgttctgga atactcacgt gagggaaactt 120
actttggcca gcattgacct tcaaagtcag atggaaccca ggacccatcc aacttggttg 180
cttcacattt tcatccctc ctgcatcatt gctttcattt tcatagccac agtgatagcc 240
ctaagaaaac aactctgtca aaagctgtat tcttcaaaag acacaacaaa aagacctgtc 300

```

accacaacaa agagggaagt gaacagtgt gtgaatctga acctgtggtc ttgggagcca 360
gggtgacctg atatgacatc taaagaagct tctggactct g 401

<210> 265
<211> 271
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(271)
<223> n = A,T,C or G

<400> 265
gccacttctt gtggacatgg gcagagcgt gctgccagtt cctggtagcc ttgaccacna 60
cgctgggggg tctttgtgat ggtcatgggt ctcatttgca cttgggggtg tgggattcaa 120
gttagaagtt tctagatctg gccgggcgca gtgggtcaca cctgtaatcc cagcacttta 180
ggaggctgag gcaggcggat catgagggtca ggagatcgag accgtccttg ctaacacagt 240
gaaacccgt ctctactaaa aatacaaaaa a 271

<210> 266
<211> 401
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

<400> 266
attcataaat ttagctgaaa gatactgatt caatttgtat acagngaata taaatgagac 60
gacagcaaaa ttttcatgaa atgtaaaata tttttatagt ttgttcatac tatatgaggt 120
tctattttta atgactttct ggattttaaa aaatttcttt aaatacaatc atttttgtaa 180
tattttattt atgcttatga tctagataat tgcagaatat cattttatct gactctgtct 240
tcataagaga gctgtggcgg aattttgaac atctgttata gggagtgatc aaattagaag 300
gcaatgtgga aaaacaattc tgggaaagat ttctttatat gaagtccttg ccactagcca 360
gccatcctaa ttgatgaaag ttatctgttc acaggcctgc a 401

<210> 267
<211> 401
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

<400> 267
gaagaggcat cacctgatcc cggagacctt tggagttaag aggcggcgga agcgagggcc 60
tgtggagtcg gatcctcttc ggggtgagcc agggtcggcg cgcgcggctg tctcanaact 120
catgcagctg ttcccgcgag gcctgtttga ggacgcgctg ccgcccatcg tgctgaggag 180
ccaggtgtac agccttgtgc ctgacaggac cgtggccgac cggcagctga aggagcttca 240
agagcanggg gagacaaat cgtccagctg ggcttcnact tggatgccca tgggaanttat 300

tctttcnctt ganggactta cnngggaccc aagaancctt tncaaggggc ccttngtgga 360
 tgggnccccga aaccnnta tttgcccttg ggggggncca a 401

<210> 268
 <211> 223
 <212> DNA
 <213> Homo sapien

<400> 268
 tcgccatgtt ggccaggctg gtcttgaact cctgacttta agtgatccac ccgcctcaac 60
 ctcccaaagt gctgggatta caggtgtgag ccaccgcgcc tggcctgata catactttta 120
 gaatcaagta gtcacgcact ttttctgttc atttttctaa aaagtaaata tacaaatgtt 180
 ttgttttttg ttttttttgt ttgtttgttt ctgttttttt ttt 223

<210> 269
 <211> 401
 <212> DNA
 <213> Homo sapien

<400> 269
 actatgtaaa ccacattgta ctttttttta ctttggcaac aaatatttat acatacaaga 60
 tgctagtcca tttgaatatt tctcccaact tatccaagga tctccagctc taacaaaatg 120
 gtttattttt atttaaagt caatagtgtt tttttaaaat ccaaatacaga ggtgcaggcc 180
 accagttaaa tgccgtctat caggttttgt gccttaagag actacagagt caaagctcat 240
 ttttaaagga gtaggacaaa gttgtcacag gtttttgttg ttgtttttat tgcccccaaa 300
 attacatgtt aatttccatt tatatcaggg attctattta cttgaagact gtgaagttgc 360
 cattttgtct cattgttttc tttgacataa ctaggatcca t 401

<210> 270
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 270
 tggctgttga ttcacctcag cactgcttgg tatctgcacc ctacctctct ttagaggctg 60
 ccttgtcaac tgaaaaatgc acctgacttc gagcaagact ctttccttag gttctggatc 120
 tgtttgagcc ccatggcact gagctggaat ctgagggtct tgttccaagg atgtgatgat 180
 gtgggagaat gttctttgaa agagcagaaa tccagtctgc atggaaacag cctgtagagn 240
 agaagtttcc agtgataagt gttcactgtt ctaaggaggt acaccacagc tacctgaatt 300
 ttcccaaaat gagtgttct gtgogttaca actggccttt gtacttgact gtgatgactt 360
 tgttttttct tttcaattct anatgaacat gggaaaaaat g 401

<210> 271
 <211> 329
 <212> DNA
 <213> Homo sapien

<400> 271
 ccacagcctc caagtcaggt ggggtggagt ccagagctg cacagggttt ggcccaagtt 60
 tctaaggag gcaattctc cctcgccea tcagtccag cccctgctgg ctggtgctg 120

```

agcccctcag acagccccct gccccgcagg cctgccttct cagggacttc tgcggggcct      180
gaggcaagcc atggagttag acccaggagc cggacacttc tcaggaaatg gcttttccca      240
acccccagcc cccaccgggt gggttcttct gttctgtgac tgtgtatagt gccaccacag      300
cttatggcat ctcattgagg acaaaaaaaa                                329

```

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<210> 272
<211> 401
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (401)
<223> n = A,T,C or G

```

```

<400> 272
nggctgntaa cntcggaggt nacttcctgg actatcctgg agacccccctc cgcttccacg      60
nncatnatac cntcatnngc tgggcccctn angacacnat cccactccaa cacctgngng      120
atgctggncn cctnggaacc anentcagaa ngacctgnt cntntgtntt ccgcaanctg      180
aagnnaangc gggntacacc tnentgcant ggnccacnct gcnnggaact ntacacacct      240
acgggatgtg gctgcgccan gagccaagag cntttctgga tgattcccca gcctcttgnn      300
agggantcta caacattgct nnntaccttt ntcnnncngc nnntnntgga ntacaggngn      360
tnntaacact acatcttttt tactgncnccn tncttgggtgg g                                401

```

```

<210> 273
<211> 401
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (401)
<223> n = A,T,C or G

```

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<400> 273
cagcaccatg aagatcaaga tcatcgcacc cccagagcgc aagtactcgg tgtggatcgg      60
tggctccatc ctggcctcac tgtccacctt ccagcagatg tggattagca agcaggagta      120
cgacgagtcg ggcccctcca tcgtccaccg caaatgcttc taaacggact cagcagatgc      180
gtagcatatt ctgcatgggt taattgagaa tagaaatttg cccctggcaa atgcacacac      240
ctcatgctag cctcacgaaa ctggaataag ccttcgaaaa gaaattgtcc ttgaagcttg      300
tatctgatat cagcactgga ttgtagaact tgttgctgat tttagacctg tattgaagtt      360
aactgttccc cttggtatta acgtgtcagg gctgagtgnt c                                401

```

```

<210> 274
<211> 401
<212> DNA
<213> Homo sapien

```

```

<400> 274
ccaccacac ccaccgcgcc ctcgttcgcc tcttctccgg gagccagtcg gcgccaccgc      60
cgccgcccag gccatcgcca cctccgcag ccatgtccac caggtccgtg tctctgtcct      120
cctaccgcag gatgttcggc ggcccgggca ccgcgagccg gccgagctcc agccggagct      180
acgtgactac gtccaccgc acctacagcc tgggcagcgc gctgcgcccc agcaccagcc      240
gcagcctcta cgctcgtcc ccgggcggcg tgtatgccac gcgctcctct gccgtgcgcc      300
tgccggagcag cgtgcccggg gtgcggctcc tgcaggactc ggtggacttc tcgctggccc      360

```

acgccatcaa caccgagttc aagaacaccc gcaccaacga g 401

<210> 275
 <211> 401
 <212> DNA
 <213> Homo sapien

<400> 275
 ccacttccac cactttgtgg agcagtgcct tcagcgcaac ccggatgcca ggtatccctg 60
 ctggcctggg cctgggcttc gggagagcag aggggtgctca ggagggttaag gccaggggtg 120
 gaagggactt acctcccaaa ggttctgcag ggggaatctgg agctacacac aggagggatc 180
 agtcctctggg tgtgtcagag gccagcctgg ggagctctgg cactgcttc ccatgagctg 240
 agggagaggg agaggggacc cgaggctgag gcataagtgg caggatttcg ggaagctggg 300
 gacacggcag tgatgctgcg gtctctcctc ccctttccct ccaggcccag tgccagcacc 360
 ctctgaacc actctttctt caagcagatc aagcgacgtg c 401

<210> 276
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 276
 tctgatattg ntacccttga gccacctaag ttagaagaaa ttggaaatca agaagttgtc 60
 attgttgaag aagcacagag ttcagaagac tttaacatgg gctcttcctc tagcagccag 120
 tatactttct gtcagccaga aactgtattt tcattctcagc ctagtgtatga tgaatcaagt 180
 agtgatgaaa ccagtaatca gcccagtcct gccttttagac gacgccgtgc taggaagaag 240
 accgtttctg cttcagaatc tgaagaccgg ctagtgtgtg aacaagaaac tgaaccttct 300
 aaggagttga gtaaactgtca gttcagtagt ggtctcaata agtgtgttat acttgctttg 360
 gtgattgcaa tcagcatggg atttggccat ttctatggca c 401

<210> 277
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 277
 aactttggca acatatctca gcaaaaacta cagctatgtt attcatgccca aaataaaaagc 60
 tgtgcagagg agtggctgca atgaggtcac aacgggtggg gatgtaaaag agatcttcaa 120
 gtcctcatca cccatccctc gaactcaagt cccgctcatt acaaattctt cttgccagtg 180
 tccacacatc ctgccccatc aagatgttct catcatgtgt tacgagnggc gctcaaggat 240
 gatgcttctt gaaaattgct tagttgaaaa atggagagat cagcttagta aaagatccat 300
 acagtgggaa gagaggctgc aggaacagcg ganaacagtt caggacaaga agaaaacagc 360
 cgggcgcacc agtcgtagta atccccccaa accaaaggga a 401

<210> 278

<211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 278
 aatgagtgtg agaccacaaa tgaatgccgg gaggatgaaa tgtgttggaa ttatcatggc 60
 ggcttccgtt gttatccacg aaatccttgt caagatccct acattctaac accagagAAC 120
 cgatgtgttt gcccgagtc aaatgccatg tgcccgagAAC tgcccgagtc aatagtctac 180
 aaatacatga gcatccgagc tgataggtct gtgccatcag acatcttcca gatacaggcc 240
 acaactatTT atgccaacac catcaatact tttcggatta aatctggaaa tgaaaatgga 300
 gagtctacct acgacaacaa anccctgtaa gtgcaatgct tgtgctcgtg aagncattat 360
 caggaccaag agaacatatc gtggacctgg agatgctgac a 401

<210> 279
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 279
 aaattattgc ctctgatata tacctaagtn aacanaacat taatacctaa gtaaacataa 60
 cattaacttg agggttgcag nttctaantg aaactgtatt tgaaactttt aagtatactt 120
 taggaacaaa gcatgaacgg cagtctagaa taccagaaac atctacttgg gtagcttggn 180
 gccattatcc tgtggaatct gatatgtctg gnagcatgtc attgatggga catgaagaca 240
 tctttggaaa tgatgagatt atttcctgtg ttaaaaaaaaa aaaaaatctt aaattcctac 300
 aatgtgaaac tgaaactaat aattttgatc ctgatgtatg ggacagcgta tctgtaccag 360
 gctctaaata acaaaagnta gggngacaag nacatgttcc t 401

<210> 280
 <211> 326
 <212> DNA
 <213> Homo sapien

<400> 280
 gaagtggAat tgtataattc aattcgataa ttgatctcat gggctttccc tggaggaaag 60
 gttttttttg ttgttttttt ttttaagaact tgaaacttgt aaactgagat gtctgtagct 120
 tttttgcccc tctgtagtgt atgtgaagat ttcaaaacct gagagcactt tttctttgtt 180
 tagaattatg agaaaggcac tagatgactt taggatttgc atttttcctt ttattgcctc 240
 atttcttgtg acgccttgtt ggggagggaa atctgtttat tttttcctac aaataaaaag 300
 ctaagattct atatcgcaaa aaaaaa 326

<210> 281
 <211> 374
 <212> DNA
 <213> Homo sapien

```

<400> 281
caacgcggttt gcaaatatc ccctggtagc ctacttcctt acccccgaat attggtaaga      60
tcgagcaatg gcttcaggac atgggttctc ttctcctgtg atcattcaag tgctcaactgc      120
atgaagactg gcttgtctca gtgtttcaac ctcaccaggg ctgtctcttg gtccacacct      180
cgctccctgt tagtgccgta tgacagcccc catcaaatga ccttggccaa gtcacggttt      240
ctctgtggtc aagggttggtt ggctgattgg tggaaagtag ggtggaccaa aggaggccac      300
gtgagcagtc agcaccagtt ctgcaccagc agcgcctccg tctagtggg tgttctctgt      360
tctctgggcc ctgg                                     374

```

```

<210> 282
<211> 404
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (404)
<223> n = A,T,C or G

```

```

<400> 282
agtgtggtgg aattcccga tcctanncgc cgactcacac aaggcagagt ngccatggag      60
aaaattccag tgtcagcatt cttgtctctt gtggccctct cctacactct ggccagagat      120
accacagtca aacctgnagc caaaaaggac acaaaggact ctcgacccaa actgccccan      180
accctctcca gaggttgggg tgaccaactc atctggactc anacatatga agaagctcta      240
tataaatcca agacaagcaa caaaccttg atgattatc atcacttgga tgagtgccca      300
cacagtcaag ctttaaagaa agtgtttgct gaaaataaag aaatccagaa attggcagag      360
cagtttgtcc tctcaatct ggtttatgaa acaactgaca aaca                                     404

```

```

<210> 283
<211> 184
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (184)
<223> n = A,T,C or G

```

```

<400> 283
agtgtggtgg aattcacttg cttaanttgt gggcaaaaga gaaaaagaag gattgatcag      60
agcattgtgc aatacagttt cattaactcc ttccctcgct cccccaaaaa tttgaatttt      120
tttttcaaca ctcttacacc tgttatggaa aatgtcaacc tttgtaagaa aacccaaaata      180
aaaa                                     184

```

```

<210> 284
<211> 421
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (421)
<223> n = A,T,C or G

```

```

<400> 284

```

```

ctattaatcc tgccacaata tttttaatta cgtacaaaga tctgacatgt caccagggga      60
cccatthcac ccaactgctct gtttgccgc cagtcttttg tctctctctt cagcaatggg      120
gaggcgata ccccttcctc ggggaanana aatccatggg ttgttgccct tgccaataac      180
aaaaatggtg gaaagtcgag tggcaaagct gttgccattg gcatctttca cgtgaaccac      240
gtcaaaagat ccagggtgcc tctctctggt ggtgatcaca ccaattcttc ctaggttagc      300
acctccagtc accatacaca gggtaccagt gtcgaaacttg atgaaatcag taatcttgcc      360
agtctctaaa tcaatctgaa tggtatcatt caccttgatg aggggatcgg ggtagcggat      420
g

```

<210> 285

<211> 361

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(361)

<223> n = A,T,C or G

<400> 285

```

ctgggtggta actctttatt tcattgtccg gaanaaagat gggagtggga acagggtgga      60
cactgtgcag gcttcagctt ccactccggg caggattcag gctatctggg accgcaggga      120
ctgccagggtg cacagccctg gctcccgagg caggcaggca aggtgacggg actggaagcc      180
cttttcanag ccttgaggga gctgggtccg ccacaagcaa tgagtgccac tctgcagttt      240
gcaggggatg gataaacagg gaaacactgt gcattcctca cagccaacag tgtaggtctt      300
ggtgaagccc cggcgctgag ctaagctcag gctgttccag ggagccacga aactgcaggt      360
a

```

<210> 286

<211> 336

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(336)

<223> n = A,T,C or G

<400> 286

```

tttgagtggc agcgccttta tttgtggggg ccttcaaggg agggtcgtgg ggggcagcgg      60
ggaggaanag ccganaaact gtgtgaccgg ggcctcaggt ggtgggcatt gggggctcct      120
cttgcanatg ccatttgga tcaccgggtgc agccattggg ggcagcgggt accggtcctt      180
tcttgttcaa catagggtag gtggcagcca cgggtccaac tcgcttgagg ctgggccctg      240
ggcgctccat tttgtgttcc angagcatgt ggttctgtgg cgggagcccc acgcaggccc      300
tgaggatggt ctcgatgcag ctgcgctggc ggaaaaa

```

<210> 287

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 287

tggttaccaa	atttntttat	ttgaaggaat	ggnacaaatc	aaanaactta	agnggatgtt	60
ttggtacaac	ttatanaaaa	ggnaaaggaa	accccaacat	gcatgcnctg	ccttgngac	120
caggaagtc	acccacggc	tatggggaaa	ttancccgag	gcttancttt	cattatcact	180
gtctcccagg	gngngcttgt	caaaaanata	ttccnccaag	ccaaattcgg	gcgctcccat	240
nttgcnaag	ttggtcacgt	ggtcacccaa	ttctttgatg	gctttcacct	gtcattcag	300
g						301

<210> 288

<211> 358

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (358)

<223> n = A,T,C or G

<400> 288

aagtttttaa	actttttatt	tgcatattaa	aaaaattgng	cattccaata	attaaaatca	60
tttgaacaaa	aaaaaaaaatg	gcactctgat	taaactgcat	tacagcctgc	aggacacctt	120
gggccagctt	ggttttactc	tanatttcac	tgctgctcca	ccccacttct	tccacccac	180
ttcttccttc	accaacatgc	aagttcttct	cttccctgcc	agccanata	atagacagat	240
gggaaaggca	ggcgcgccct	tcgttgctcag	tagttctttg	atgtgaaagg	ggcagcacag	300
tcatttaaac	ttgatccaac	ctctttgcat	cttacaaagt	taaacagcta	aaagaagt	358

<210> 289

<211> 462

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (462)

<223> n = A,T,C or G

<400> 289

ggcatcagaa	atgctgttta	tttctctgct	gctcccaagc	tggttgccct	ttgcagagga	60
gcagacaaca	gatgcatagt	tgggganaaa	gggaggacag	gttccaggat	agaggggtgca	120
ggctgagga	ggaagggtaa	naggaaggaa	ggccatcctg	gatccccaca	tttcagtctc	180
anatgaggac	aaagggactc	ccaagcccc	aatcatcan	aaaacaccaa	ggagcaggag	240
gagcttgagc	aggccccagg	gagcctcana	gccataccag	ccactgtcta	cttcccatcc	300
tcctctccca	ttccctgtct	gcttcanacc	acctccagc	taagccccag	ctccattccc	360
ccaatcctgg	cccttgccag	cttgacagtc	acagtgcctg	gaattccacc	actgaggctt	420
ctcccagttg	gattaggacg	tcgcctgtt	agcatgctgc	cc		462

<210> 290

<211> 481

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (481)

<223> n = A,T,C or G

<400> 290

tacttttccta	aacttttatta	aagaaaaaag	caataagcaa	tggnnggtaaa	tctctanaac	60
ataccaatt	ttctgggctt	cctccccga	gaatgtgaca	ttttgatttc	caaacatgcc	120
anaagtgtat	ggttcccaac	tgtactaaag	taggtganaa	gctgaagtcc	tcaagtgttc	180
atcttccaac	ttttccagc	ctgtgggtctg	tctttggatc	agcaataatt	gcctgaacag	240
ctactatggc	ttcggtgatt	tttgtctgta	gctctctgag	ctcctctatg	tgcagcaatc	300
gcanaatttg	agcagcttca	ttaanaactg	catctcctgt	gtcaaaaacca	anaatatgtt	360
tgtctaaagc	aacaggtaag	ccctcttttg	tttgatttgc	cttancaact	gcacccctgtg	420
tcaggcgctc	ctgaaccaa	atccgaattg	ccttaagcat	taccaggtaa	tcatcatgac	480
g						481

<210> 291

<211> 381

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(381)

<223> n = A,T,C or G

<400> 291

tcataagtaat	gtaaaaccat	ttgtttaatt	ctaaatcaaa	tcactttcac	aacagtgaag	60
attagtgtact	ggttaaggng	tgccactgta	catatcatca	ttttctgact	gggggtcagg	120
cctgggtccta	gtccacaagg	gtggcaggag	gaggggtggag	gctaanaaca	cagaaaacac	180
acaaaanaaa	ggaaagctgc	cttggcnaaa	ggatgaggng	gtgagcttgc	cgaaggatgg	240
tggaagggg	gctccctgtt	ggggccgagc	caggagtccc	aagtcagctc	tcctgcctta	300
cttagctcct	ggcanagggt	gagtggggac	ctacgagggt	caaaatcaaa	tggcatttgg	360
ccagcctggc	tttactaaca	g				381

<210> 292

<211> 371

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(371)

<223> n = A,T,C or G

<400> 292

gaaaaaataa	tcggtttaat	tgaaaaacct	gnaggatact	attccactcc	cccanatgag	60
gaggctgagg	anaccaaacc	cctacatcac	ctcgtagcca	cttctgatac	tcttcacgag	120
gcagcaggca	aagacaattc	ccaaaacctc	nacaaaagca	attccaaggg	ctgctgcagc	180
taccaccanc	acatttttcc	tcagccagcc	cccaatcttc	tccacacagc	cctccttatg	240
gatcgcttcc	tcggttgaaat	taatcccaca	gccacagta	acattaatgc	ancaggagtc	300
ggggactcgg	ttcttcgaca	tggaagggat	tttctcccaa	tctgtgtagt	tagcagcccc	360
acagcactta	a					371

<210> 293

<211> 361

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (361)
 <223> n = A,T,C or G

<400> 293
 gattttaaag aaaacacttt attgttcagc aattaaaagt tagccaaata tgtatttttc 60
 tccataattt attgngatgt tatcaacatc aagtaaaatg ctcatTTtca tcatttgctt 120
 ctgttcatgt tttcttgaac acgtcttcaa ttttccttcc aaaatgctgc atgccacact 180
 tgaggtaacg aagcanaagt atttttaaac atgacagcta anaacattca tctacagcaa 240
 cctatatgct caatacatgc cgcgtgatcc tagtagtttt ttcacaacct tctacaagtt 300
 tttggaaaac atctgttatg atgactttca tacaccttca cctcaaaggc tttcttgcac 360
 c 361

<210> 294
 <211> 391
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (391)
 <223> n = A,T,C or G

<400> 294
 tatttttaaag tttaattatg attcanaaaa aatcgagcga ataactttct ctgaaaaaat 60
 atattgactc tgtatanacc acagttattg gggganaagg gctggtaggt taaattatcc 120
 tattttttat tctgaaaatg atattaatan aaagtcccgt ttccagtctg attataaaga 180
 tacatatgcc caaaatggct ganaataaat acaacaggaa atgcaaaagc tgtaaagcta 240
 agggcatgca ananaaaatc tcanaatacc caaagnggca acaaggaacg tttggctgga 300
 atttgaagtt atttcagtca tctttgtctt tggctccatg tttcaggatg cgtgtgaact 360
 cgatgtaatt gaaattcccc tttttatcaa t 391

<210> 295
 <211> 343
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (343)
 <223> n = A,T,C or G

<400> 295
 ttcttttggt ttattgataa cagaaactgt gcataattac agatttgatg aggaatctgc 60
 aaataataaa gaatgtgtct actgccagca aaatacaatt attccatgcc ctctcaacat 120
 acaaatatag agttcttcac accanattggc tctgggtgtaa caaagccatt ttanatgttt 180
 aattgtgctt ctacaaaacc ttcanagcat gaggtagttt cttttacctt cnatattttc 240
 cacatttcca ttattacact tttagtgagc taaaatcctt ttaacatagc ctgcggatga 300
 tctttcacaa aagccaagcc tcattttcaa agggtttatt tct 343

<210> 296
 <211> 241
 <212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (241)

<223> n = A,T,C or G

<400> 296

ttcttggata ttggttgttt ttgtgaaaaa gtttttgttt ttcttctcag tcaactgaat	60
tattttctcta ctttgccctc ctgatgcccc catgananaa cttaanataa tttctaacag	120
cttccacttt ggaaaaaaaa aaaacctgtt ttccctcatgg aaccccagga gttgaaagtg	180
gatanatcgc tctcaaaatc taaggctctg ttcagcttta cattatgtta cctgacgttt	240
t	241

<210> 297

<211> 391

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (391)

<223> n = A,T,C or G

<400> 297

gttgtggctg anaatgctgg agatgctcag ttctctccct cacaaggtag gccacaaatt	60
cttgggtggtg ccctcacatc tggggctctc aggcaccagc catgcctgcc gaggagtgtc	120
gtcaggacan accatgtccg tgctaggccc aggcacagcc caacctctcc tcatccaagt	180
ctctcccagg tttctgggtc cgatgggcaa ggatgacccc tccagtggct ggtacccac	240
catcccacta cccctcacat gctctcactc tccatcaggt ccccaatcct ggcttccctc	300
ttcacgaact ctcaaagaaa aggaaggata aaacctaaat aaaccagaca gaagcagctc	360
tggaaaagta caaaaagaca gccagaggtg t	391

<210> 298

<211> 321

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (321)

<223> n = A,T,C or G

<400> 298

caagccaaac tgtntccagc tttatttaaan atactttcca taaacaatca tggattttca	60
ggcaggacat gggcanacaa tcgttaacag tatacacaaa ctttcaaact cccttnttca	120
atggactacc aaaaatcaaa aagccactat aaaacccaat gaagtcttca tctgatgtc	180
tgaacaggga aagtttaaag ngagggttga catttcacat ttagcatgtt gtttaacaac	240
ttttcacaag ccgaccctga ctttcaggaa gtgaaatgaa aatggcanaa tttatctgaa	300
natccacaat ctaaaaatgg a	321

<210> 299

<211> 401

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 299
 tatcataaag agtggtgaag tttatattt atagcaccat tgagacattt tgaaattgga 60
 attggtaaaa aaataaaaca aaaagcattt gaattgtatt tggnggaaca gcaaaaaaag 120
 agaagtatca tttttctttg tcaaattata ctgtttccaa acattttgga aataaataac 180
 tggaattttg tcggtcactt gcaactggtt acaagattag aacaagagga acacatatgg 240
 agttaaat tttttgttgg gatttcana agagtttggg ttataaaaag caaacagggc 300
 caacgtccac accaaaattct tgatcaggac caccaatgtc atagggngca atatctacaa 360
 taggtagtct cacagccttg cgtgttcgat attcaaagac t 401

<210> 300
 <211> 188
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(188)
 <223> n = A,T,C or G

<400> 300
 tgaatgcttt gtcataatga gaaagttaaa gtgcaataat gtttgaanac aataagtggg 60
 ggtgtatctt gttttctaata agataaactt ttttgtcttt gctttatctt attaggggag 120
 tgtatgtcag tgtataaaac atactgtgtg gtataacagg cttataaat tctttaaaag 180
 gaaaaaaa 188

<210> 301
 <211> 291
 <212> DNA
 <213> Homo sapien

<400> 301
 aagattttgt tttatattt tatggctaga aagacactgt tatagccaaa atcggcaatg 60
 acactaaaga aatcctctgt gcttttcaat atgcaaata atttcttcca agagttgccc 120
 tgggtgtgact tcaagagttc atgttaactt cttttctgga aacttccttt tcttagttgt 180
 tgtattcttg aagagcctgg gccatgaaga gcttgcceta gttttgggca gtgaactcct 240
 tgatgttctg gcagtaagtg tttatctggc ctgcaatgag cagcgagtcc a 291

<210> 302
 <211> 341
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(341)
 <223> n = A,T,C or G

<400> 302
 tgatttttca taattttatt aaatnatcac tgggaaaact aatgggttcgc gtatcacaca 60


```

attacactac aatctgatag gagtggtaaa accagccaat ggaatccagg taaagtacaa      120
aaacgccacc ttttattgtc ctgtcttatt tctcggaag gagggttcta ctttacacat      180
ttcatgagcc agcagtggac ttgagttaca atgtgtaggt tccttgtagt tatagctgca      240
gaagaagcca tcaaattctt gaggacttga catctctcgg aaagaagcaa actagtggat      300
ccccggggt gcaggaattc gatatcaagc ttatcgatac c                             361

```

```

<210> 303
<211> 361
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(361)
<223> n = A,T,C or G

```

```

<400> 303
tgcagacagt aaatnaattt tatttngngtt cacagaacat actaggcgat ctcgacagtc      60
gctccgtgac agcccaccaa cccccaaccc tntacctcgc agccacccta aaggcgactt      120
caanaanatg gaaggatctc acggatctca ttctaattgg tccgccgaag tctcacacag      180
tanacagacg gagttganat gctggaggat gcagtcacct cctaaactta cgaccacca      240
ccanacttca tcccagccgg gacgtcctcc cccacccgag tcttccccat ttcttctcct      300
actttgccgc agttccaggc gtcctgcttc caccagtccc acaaagctca ataaatacca      360
a                             361

```

```

<210> 304
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 304
ctctttacaa cagcctttat ttneggcctt tgatcctgct cggatgctgg tggaggccct      60
tagctccgcc cgccaggctc tgtgccgctt ccccgaggc gcanattcat gaacacgggtg      120
ctcaggggct tgaggcgcta ctccccagc gggagctggt cctccagggg cttcccctcg      180
aaggtcagcc anaacaggtc gtctgcaca cctccagcc cgctcacttg ctgcttcagg      240
tgggccacgg tctgcgtcag ccgcacctcg taggtgctgc tgcggccctt gttattcctc      300
a                             301

```

```

<210> 305
<211> 331
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(331)
<223> n = A,T,C or G

```

```

<400> 305
ganaggctag taacatcagt tttattgggt tggggnggca accatagcct ggctgggggn      60

```

ggggctggcc	ctcacagggt	gttgagttcc	agcagggtct	ggccaaggt	ctggtgaatc	120
tcgacgttct	cctccttggc	actggccaag	gtctcttcta	ggcatcgat	ggttttctcc	180
aactttgcca	canacctctc	ggcaaactct	gctcgggtct	cancctcctt	cagcttctcc	240
tccaacagtt	tgatctcctc	ttcatattta	tcttcttggg	gggaatactc	ctcctctgag	300
gccatcaggg	acttgagggc	ctggtccatg	g			331

<210> 306
 <211> 457
 <212> DNA
 <213> Homo sapien

<400> 306						
aatatgtaaa	ggtaataact	tttattatat	taaagacaat	gcaaacgaaa	aacagaattg	60
agcagtgcaa	aatttaaagg	actgttttgt	tctcaaagtt	gcaagtttca	aagccaaaag	120
aattatatgt	atcaaatata	taagtaaaaa	aaagttagac	tttcaagcct	gtaatccag	180
cactttggga	ggctgaggca	ggtggatcac	taacattaaa	aagacaacat	tagattttgt	240
cgatttatag	caattttata	aatatataac	tttgtcactt	ggatcctgaa	gcaaaataat	300
aaagtgaatt	tgggattttt	gtacttggtg	aaaagtttaa	caccctaaat	tcacaactag	360
tggatcccc	gggctgcagg	aattcgatat	caagcttata	gataccgtcg	acctcgaggg	420
ggggcccggt	acccaattcg	ccctatagtg	agtcgta			457

<210> 307
 <211> 491
 <212> DNA
 <213> Homo sapien

<400> 307						
gtgcttggac	ggaacccggc	gctcgttccc	caccccggcc	ggccgcccac	agccagccct	60
ccgtcacctc	ttcacgcac	cctcggactg	ccccaggcc	cccgcgcgcg	ctccagcgcc	120
gcgcagccac	cgccgcgcgc	gcccctctc	cttagtcgcc	gccatgacga	ccgcgtccac	180
ctcgcagggt	cgccagaact	accaccagga	ctcagaggcc	gccatcaacc	gccagatcaa	240
cctggagctc	tacgcctcct	acgtttacct	gtccatgtct	tactactttg	accgcgatga	300
tgtggctttg	aagaactttg	ccaaataactt	tcttcaccaa	tctcatgagg	agaggggaaca	360
tgctgagaaa	ctgatgaagc	tgcagaacca	acgagggtggc	cgaatcttcc	ttcaggatat	420
caagaaacca	gactgtgatg	actgggagag	cgggctgaat	gcaatggagt	gtgcattaca	480
tttggaaaaa	a					491

<210> 308
 <211> 421
 <212> DNA
 <213> Homo sapien

<400> 308						
ctcagcgctt	cttctttctt	ggtttgatcc	tgactgctgt	catggcggtgc	cctctggaga	60
aggccctgga	tgtgatggtg	tccaccttcc	acaagtactc	gggcaaagag	ggtgacaagt	120
tcaagctcaa	caagtcagaa	ctaaaggagc	tgctgacccg	ggagctgccc	agcttcttgg	180
ggaaaaggac	agatgaagct	gctttccaga	agctgatgag	caacttggac	agcaacaggg	240
acaacgaggt	ggacttccaa	gagtactgtg	tcttcctgtc	ctgcacgcgc	atgatgtgta	300
acgaattctt	tgaaggcttc	ccagataagc	agcccaggaa	gaaatgaaaa	ctcctctgat	360
gtgggtgggg	ggtctgccag	ctggggccct	ccctgtcgcc	agtgggcact	tttttttttc	420
c						421

<210> 309
 <211> 321
 <212> DNA

<213> Homo sapien

<400> 309

accaaattggc	ggatgacgcc	ggtgcagcgg	gggggcccgg	gggccctggt	ggccctggga	60
tggggaaccg	cgggtggcttc	cgcggaggtt	tcggcagtgg	catccggggc	cggggctcgcg	120
gccgtggacg	gggcccgggc	cgaggccgcg	gagctcgcgg	aggcaaggcc	gaggataagg	180
agtggatgcc	cgtcaccaag	ttgggcccgt	tggtcaagga	catgaagatc	aagtcctcgg	240
aggagatcta	tctcttctcc	ctgcccatta	aggaatcaga	gatcattgat	ttcttctcgg	300
gggcctctct	caaggatgag	g				321

<210> 310

<211> 381

<212> DNA

<213> Homo sapien

<400> 310

ttaaccagcc	atattggctc	aataaatagc	ttcggtaagg	agttaatttc	cttctagaaa	60
tcagtgccta	tttttcctgg	aaactcaatt	ttaaatagtc	caattccatc	tgaagccaag	120
ctgttgatcat	tttcattcgg	tgacattctc	tcccatgaca	cccagaaggg	gcagaagaac	180
cacatttttc	atztatagat	gtttgcatcc	tttgtattaa	aattattttg	aaggggttgc	240
ctcattggat	ggcttttttt	tttttcctcc	agggagaagg	ggagaaatgt	acttggaaat	300
taatgtatgt	ttacatctct	ttgcaaatcc	ctgtacatag	agatatattt	tttaagtgtg	360
aatgtaacaa	catactgtga	a				381

<210> 311

<211> 538

<212> DNA

<213> Homo sapien

<400> 311

tttgaattta	caccaagaac	ttctcaataa	aagaaaatca	tgaatgctcc	acaattttcaa	60
cataccacaa	gagaagttaa	tttcttaaca	ttgtgttcta	tgattatttg	taagaccttc	120
accaagtctc	gatattcttt	aaagacatag	ttcaaaattg	cttttgaaaa	tctgtattct	180
tgaaaatata	cttgttgtgt	attaggtttt	taaataccag	ctaaaggatt	acctcactga	240
gtcatcagta	ccctcctatt	cagctcccca	agatgatgtg	tttttgctta	ccctaagaga	300
ggttttcttc	ttatttttag	ataattcaag	tgcttagata	aattatgttt	tctttaagtg	360
tttatggtaa	actcttttaa	agaaaattta	atatgttata	gctgaatctt	tttggtaact	420
ttaaatcttt	atcatagact	ctgtacatat	gttcaaatta	gctgcttgcc	tgatgtgtgt	480
atcatcggtg	ggatgacaga	acaaacatat	ttatgatcat	gaataatgtg	ctttgtaa	538

<210> 312

<211> 176

<212> DNA

<213> Homo sapien

<400> 312

ggaggagcag	ctgagagata	gggtcagtga	atgcggttca	gcctgctacc	tctcctgtct	60
tcatagaacc	attgccttag	aattattgta	tgacacgttt	tttgttggtt	aagctgtaag	120
gtttttgtct	ttgtgaacat	gggtattttg	agggggagggt	ggaggaggta	gggaag	176

<210> 313

<211> 396

<212> DNA

<213> Homo sapien

<400> 313

ccagcacc	ccccc	caggccct	ggg	acctggg	ttctcagact	gccaaagaag	ccttgccatc	60
tggcgctccc	atggctcttg	caacatctcc	ccttcgtttt	tgaggggggtc	atgccggggg			120
agccaccagc	ccctcactgg	gttcgggagga	gagtcaggaa	gggccaagca	cgacaaagca			180
gaaacatcgg	atttggggaa	cgcggtgtcaa	tcccttggtgc	cgcaggggtg	ggcgggagag			240
actgtttctgt	tccttggtgta	actgtgttgc	tgaaagacta	cctcgttctt	gtcttgatgt			300
gtcaccggggg	caactgcctg	ggggcgggga	tgggggcagg	gtggaagcgg	ctccccattt			360
tataccaaag	gtgctacatc	tatgtgatgg	gtgggg					396

<210> 314

<211> 311

<212> DNA

<213> Homo sapien

<400> 314

cctcaacatc	ctcagagagg	actggaagcc	agtccttacg	ataaactcca	taatttatgg	60
cctgcagtat	ctcttcttgg	agcccaaccc	cgaggaccca	ctgaacaagg	aggccgcaga	120
ggctcctgcag	aacaaccggc	ggctgtttga	gcagaacgtg	cagcgctcca	tcgggggtgg	180
ctacatcggc	tccacctact	ttgagcgctg	cctgaaatag	ggttggcgca	taccacccc	240
cgccacgggcc	acaagccctg	gcatccctg	caaatatatta	ttggggggcca	tgggtagggg	300
tttgggggggc	g					311

<210> 315

<211> 336

<212> DNA

<213> Homo sapien

<400> 315

tttagaacat	ggttatcatc	caagactact	ctaccctgca	acattgaact	cccaagagca	60
aatccacatt	cctcttgagt	tctgcagctt	ctgtgtaaat	agggcagctg	tcgtctatgc	120
cgtagaatca	catgatctga	ggaccattca	tggaagctgc	taaatagcct	agtctgggga	180
gtcttccata	aagtttttgca	tggagcaaac	aaacaggatt	aaactagggt	tggttccttc	240
agccctctaa	aagcataggg	cttagcctgc	aggcttcctt	gggctttctc	tgtgtgtgta	300
gttttgtaaa	cactatagca	tctgttaaga	tccagt			336

<210> 316

<211> 436

<212> DNA

<213> Homo sapien

<400> 316

aacatgggtct	gcggtgcctta	agagagacgc	ttcctgcaga	acaggacctg	actacaaaga	60
atgtttccat	tggaattgtt	ggtaaagact	tggagtttac	aatctatgat	gatgatgatg	120
tgtctccatt	cctggaaggt	cttgaagaaa	gaccacagag	aaaggcacag	cctgctcaac	180
ctgctgatga	acctgcagaa	aaggctgatg	aaccaatgga	acattaagtg	ataagccagt	240
ctatatatgt	attatcaa	atgtaagaat	acaggcacca	catactgatg	acaataatct	300
atactttgaa	ccaaaagt	tgcagagtgg	gaatgctatg	tttttaggaat	cagtcagat	360
gtgagttttt	tccaagcaac	ctcactgaaa	cctatataat	ggaatacatt	tttctttgaa	420
agggtctgta	taatca					436

<210> 317

<211> 196

<212> DNA

<213> Homo sapien

<400> 317
 tattccttgt gaagatgata tactatTTTT gttaagcgtg tctgtattta tgtgtgagga 60
 gctgctggct tgcagtgcgc gtgcacgtgg agagctgggtg cccggagatt ggacggcctg 120
 atgctccctc ccttgccttg gtccagggaa gctggccgag ggtcctggct cctgaggggc 180
 atctgcccct ccccca 196

<210> 318
 <211> 381
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(381)
 <223> n = A,T,C or G

<400> 318
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 gccggggcgg tgcgtgaactt taagctgaaa aagaaggaca cncagggctt tggggaggag 120
 tncagggagc ccaacacagg tgacaacatc cggaattct tgcgtancct cagatacttt 180
 cnaatcttca tncctctgtg gaacatcttc atgatgttct gcatgattgt gctgntcggc 240
 tcttgaatcc cancgatgaa accannaact cactttcccg ggatgccgan tctccattcc 300
 tccattcctg atgacttcaa naatgttttt gaccaaaaaa ccgacaacct tcccagaaag 360
 tccaagctcg tgggtggngg a 381

<210> 319
 <211> 506
 <212> DNA
 <213> Homo sapien

<400> 319
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 tttgtaaata cttttgttat aattgatagg atacatcttg gacatggaat tgttaagcca 120
 cctctgagca gtgtatgtca ggacttggtc attaggttgg cagcagaggg gcagaaggaa 180
 ttatacaggt agagatgtat gcagatgtgt ccatatatgt ccatatttac attttgatag 240
 ccattgatgt atgcatctct tggctgtact ataagaacac attaatcaa tggaaataca 300
 ctttgcta attttaattg tatagatctg ctaatgaatt ctcttaaaaa catactgtat 360
 tctgttgctg tgtgtttcat tttaaattga gcattaaggg aatgcagcat ttaaatacaga 420
 actctgccaa tgcttttatc tagaggcgtg ttgccatttt tgtcttatat gaaatttctg 480
 tccaagaaa ggcaggatta catctt 506

<210> 320
 <211> 351
 <212> DNA
 <213> Homo sapien

<400> 320
 ctgacctgca ggacgaaacc atgaagagcc tgatccttct tgccatcctg gccgccttag 60
 cggtagtaac tttgtgttat gaatcacatg aaagcatgga atcttatgaa cttaatecct 120
 tcattaacag gagaaatgca aataccttca tatccctca gcagagatgg agagctaaag 180
 tccaagagag gatccgagaa cgctctaagc ctgtccacga gctcaatagg gaagcctgtg 240
 atgactacag actttgcgaa cgctacgcca tggtttatgg atacaatgct gcctataatc 300
 gctacttcag gaagcgccga gggaccaaat gagactgagg gaagaaaaaa a 351

<210> 321

<211> 421
 <212> DNA
 <213> Homo sapien

<400> 321
 ctccggaggcg ttcagctgct tcaagatgaa gctgaacatc tccttcccag ccactggctg 60
 ccagaaactc attgaagtgg acgatgaacg caaacttcgt actttctatg agaagcgtat 120
 ggccacagaa gttgctgctg acgctctggg tgaagaatgg aagggttatg tgggccgaat 180
 cagtgggtggg aacgacaaac aagggttccc catgaagcag ggtgtcttga cccatggccg 240
 tgtccgcctg ctactgagta aggggcattc ctgttacaga ccaaggagaa ctggagaaag 300
 aaagagaaaa tcagttcgtg gttgcattgt ggatgcaaat ctgagcgttc tcaacttggg 360
 tattgtaaaa aaaggagaga aggatattcc tggactgact gatactacag tgcctcgccg 420
 c 421

<210> 322
 <211> 521
 <212> DNA
 <213> Homo sapien

<400> 322
 agcagctctc ctgccacagc tcctcaccac ctgaaaatgt tcgcctgctc caagtttgtc 60
 tccactccct ccttgggtcaa gagcacctca cagctgctga gccgtccgct atctgcagtg 120
 gtgctgaaac gaccggagat actgacagat gagagcctca gcagcttggc agtctcatgt 180
 ccccttacct cacttgtctc tagccgcagc ttccaaacca gcgccatttc aagggacatc 240
 gacacagcag ccaagttcat tggagctggg gctgccacag ttgggggtggc tgggtctggg 300
 gctgggattg gaactgtgtt tgggagcctc atcattgggt atgccaggaa cccttctctg 360
 aagcaacagc tcttctccta cgccattctg ggctttgcc tctcggaggc catggggctc 420
 ttttgtctga tggtagcctt tctcatcctc tttgccatgt gaaggagccg tctccacctc 480
 ccatagtctt cccgcgtctg gttggccccg tgtgttctt t 521

<210> 323
 <211> 435
 <212> DNA
 <213> Homo sapien

<400> 323
 ccgaggtcgc acgcgtgaga cttctccgcc gcagacgccg ccgcgatgcg ctacgtcgcc 60
 tctacctgc tggctgccct agggggcaac tcctcccca gcgccaagga catcaagaag 120
 atcttggaca gcgtgggtat cgaggcggac gacgaccggc tcaacaaggt tatcagtga 180
 ctgaatggaa aaaacattga agacgtcatt gccagggta ttggcaagct tgccagtgt 240
 cctgctggtg gggctgtagc cgtctctgct gcccaggct ctgcagcccc tgctgctggt 300
 tctgcccctg ctgcagcaga ggagaagaaa gatgagaaga aggaggagtc tgaagagtca 360
 gatgatgaca tgggatttgg cctttttgat taaattcctg ctcccctgca aataaagcct 420
 ttttacacat ctcaa 435

<210> 324
 <211> 521
 <212> DNA
 <213> Homo sapien

<400> 324
 aggagatcga ctttcgggtgc ccgcaagacc agggctggaa cgccgagatc acgtgcaga 60
 tgggtgcagta caagaatcgt caggccatcc tggcggtcaa atccacgcgg cagaagcagc 120
 agcacctggt ccagcagcag cccccctcgc agccgcagcc gcagccgcag ctccagcccc 180
 aaccccagcc tcagcctcag ccgcaacccc agccccaatc acaaccccag cctcagcccc 240

aacccaagcc	tcagccccag	cagctccacc	cgtatccgca	tccacatcca	catccacact	300
ctcatcctca	ctcgcaccca	cacctccacc	cgcaccgcga	tccgcaccaa	ataccgcacc	360
cacacccaca	gccgcactcg	cagccgcacg	ggcaccggct	tctccgcagc	acctccaact	420
ctgcctgaaa	ggggcagctc	ccgggcaaga	caaggttttg	aggacttgag	gaagtgggac	480
gagcacattt	ctattgtctt	cacttggatc	aaaagcaaaa	c		521

<210> 325

<211> 451

<212> DNA

<213> Homo sapien

<400> 325

attttcat	ccattaac	ggaagcttc	atgaatat	tcttcttt	aaacatttta	60
acattatt	aacagaaaa	gatgggct	ttctggtt	ttgttacat	atagcagaga	120
tattttta	tagattact	tgggaatga	agattgttg	cttgaact	ggcactgtac	180
agtgaatg	tctgtagtt	tgttagttg	cattaagca	gtataacat	caagtatgtc	240
atccaaata	gaggcatata	cattgaattg	tttttaat	tctgacaag	tgactcttcg	300
acccccacc	ccacccaaga	cattttaata	gtaaataga	agagagagaa	gagttaatga	360
acatgagg	gtgttccact	ggcaggatga	cttttcaata	gctcaaatca	atttcagtgc	420
ctttatcact	tgaattatta	acttaatttg	a			451

<210> 326

<211> 421

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(421)

<223> n = A,T,C or G

<400> 326

cgcggtcg	ta	agggtc	gagg	at	ttttgg	tc	cg	cg	ctcc	tg	ctct	gac	tc	accg	ctgt	60
tcgctctc	gc	cgagga	acaa	gtcgg	tcagg	aagccc	gcgc	gcaac	agcca	tg	gctttt	taa				120
ggataacc	gga	aaaac	acccg	tggag	cggga	ggtgg	caatt	caccg	aattc	gaat	cacc	ct				180
aacaagcc	gc	aacgta	aaaat	ccttg	gaaaa	ggtgt	gtgct	gactt	gataa	gagg	cg	caaa				240
agaaaaga	aat	ctcaa	agtga	aagg	accagt	tcgaat	gcct	acca	agactt	tgag	antcac					300
tacaagaaa		actcct	tg	gtga	agg	ttc	taag	acgt	gg	gatc	gttt	cc	agat	gaga	aat	360
tcacaagc	ga	ctcatt	gact	tgca	cag	tc	ttct	gag	att	gtta	agcaga	ttact	ttcc	at		420
c																421

<210> 327

<211> 456

<212> DNA

<213> Homo sapien

<400> 327

atcttgac	ga	ggctgc	gg	ttctgc	tgt	ttctcc	gagc	ttcg	caatgc	cg	ctaagga		60
cgacaaga	aag	aagaag	gacg	ctggaa	agtc	ggcca	agaaa	gacaa	agacc	cagt	ga	acaa	120
atccgggg	gc	aaggcc	aaaaa	agaaga	agtg	gtccaa	aggc	aaagt	tcggg	aca	agct	caa	180
taacttag	tc	ttgttt	gaca	aagct	accta	tgataa	aactc	tgta	aggaag	ttcc	caacta		240
taaactta	tata	acccc	agctg	tggtct	ctga	gagact	gaag	attcg	aggct	ccct	ggccag		300
ggcagccc	tt	caggag	ctcc	ttagta	aaagg	acttat	caaaa	ctgg	tttcaa	agca	cagagc		360
tcaagta	att	tacacc	agaa	atacca	aggg	tggag	atgct	ccag	ctgctg	gtga	agatgc		420
atgaatag	gt	ccaacc	agct	gtacatt	ttgg	aaaaat							456

<210> 328
 <211> 471
 <212> DNA
 <213> Homo sapien

<400> 328
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 caggggaagac agggcgacct ggaagtccaa ctacttcctt aagatcatcc aactattgga 120
 tgattatccg aaatgtttca ttgtgggagc agacaatgtg ggctccaagc agatgcagca 180
 gatccgcattg tcccttcgcg ggaaggctgt ggtgctgatg ggcaagaaca ccatgatgcg 240
 caaggccatc cgagggcacc tggaaaacaa cccagctctg gagaaactgc tgcctcatat 300
 cggggggaat gtgggctttg tgttcaccaa ggaggacctc actgagatca gggacatgtt 360
 gctggccaat aaggtgccag ctgctgcccg tgctggtgcc attgccccat gtgaagtcc 420
 tgtgccagcc cagaacactg gtctcgggcc cgagaagacc tcctttttcc a 471

<210> 329
 <211> 278
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(278)
 <223> n = A,T,C or G

<400> 329
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 aaattgagat gccccccag gccagcaaat gtctcttttt gttcaaagtc tttttttatt 120
 ccttgatatt tttctttttt tttttttttt ttgnggatgg ggacttgtga atttttctaa 180
 aggtgctatt taacatggga gganagcgtg tgccggtcca gccagccccg ctgctcactt 240
 tccacctct ctccacctgc ctctggcttc tcaggcct 278

<210> 330
 <211> 338
 <212> DNA
 <213> Homo sapien

<400> 330
 ctccagcttc aacatcgaat acgcccagc ccccttcgcc ctattcttca tagccgaata 60
 cacaacatt attataataa acaccctcac cactacaatc ttctaggaa caacatatga 120
 cgcactctcc cctgaactct acacaacata ttttgtcacc aagaccctac ttctaacctc 180
 cctgttctta tgaattcgaa cagcataccc ccgattccgc tacgaccaac tcatacacct 240
 cctatgaaaa aacttctac cactcacctc agcattactt atatgatatg tctccatacc 300
 cattacaatc tccagcattc cccctcaaac ctaaaaaa 338

<210> 331
 <211> 2820
 <212> DNA
 <213> Homo sapiens

<400> 331
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 gttgtacctg gaaaacaatg cccagactca atttagtgag ccacagtaca cgaacctggg 120


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gctcctgaac agcatggacc agcagattcg gaacggctcc tegtccacca gtccctataa 180
cacagaccac gcgcagaaca gcgtcacggc gccctcgccc taegcacagc ccagccccac 240
cttcgatgct ctctctccat caccgcctat cccctccaac accgactacc caggcccgc 300
cagttccgac gtgtccttcc agcagtcgag caccgccaag tcggccacct ggacgtattc 360
cactgaactg aagaaactct actgccaaat tgcaaagaca tgccccatcc agatcaagg 420
gatgacccca cctcctcagg gagctgttat ccgcgccatg cctgtctaca aaaaagctga 480
gcacgtcacg gaggtggtga agcgggtgcc caaccatgag ctgagccgtg agttcaacga 540
gggacagatt gccctccta gtcatttgat tcgagtagag gggaacagcc atgcccagta 600
tgtagaagat cccatcacag gaagacagag tgtgtcggta ccttatgagc cccccaggt 660
tggcactgaa ttcacgacag tcttgtagaa tttcatgtgt aacagcagtt gtgttgagg 720
gatgaaccgc cgtccaattt taatcattgt tactctggaa accagagatg ggcaagtcct 780
gggcccagc gcgttttgagg ccgggatctg tgcttgccca ggaagagaca ggaaggcgga 840
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gcgcccgttt cgtcagaaca cacatggtat ccagatgaca tccatcaaga aacgaagatc 960
cccagatgat gaactgttat acttaccagt gaggggcccgt gagacttatg aaatgctgtt 1020
gaagatcaaa gaggccctgg aactcatgca gtaccttctt cagcacacaa ttgaaacgta 1080
caggcaacag caacagcagc agcaccagca cttacttcag aaacagacct caatacagtc 1140
tccatcttca tatggtaaca gctccccacc gctgaacaaa atgaacagca tgaacaagct 1200
gccttctgtg agccagctta tcaacctca gcagcgcaac gccctcactc ctacaacccat 1260
tcttgatggc atgggagcca acattcccat gatgggcacc cacatgccaa tggctggaga 1320
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<210> 332

<211> 2270

<212> DNA

<213> Homo sapiens

<400> 332

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<211> 2816

<212> DNA

<213> Homo sapiens

<400> 333

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<210> 334

<211> 2082

<212> DNA

<213> Homo sapiens

<400> 334

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<210> 335

<211> 4849

<212> DNA

<213> Homo sapiens

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<210> 336

<211> 1386

<212> DNA

<213> Homo sapiens

<400> 336

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cacagtttcg acgtgtcctt ccagcagtcg agcaccgcca agtcggccac ctggacgtat 300
tccactgaac tgaagaaact ctactgccaa attgcaaaga catgccccat ccagatcaag 360
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gagcacgtca cggagggtgt gaagcgtgtc cccaaccatg agctgagccg tgaattcaac 480
gagggacaga ttgcccctcc tagtcatttg attcgagtag aggggaacag ccatgcccag 540
tatgtagaag atcccatcac aggaagacag agtgtgctgg taccttatga gccaccccag 600
gttggaactg aattcacgac agtcttgtag aatttcattg gtaacagcag ttgtgttggg 660
gggatgaacc gccgtccaat tttaatcatt gttactctgg aaaccagaga tgggcaagtc 720
ctgggcccag gctgctttga ggcccggatc tgtgcttgcc caggaagaga caggaaggcg 780
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aagcgcccggt ttcgtcagaa cacacatggt atccagatga catccatcaa gaaacgaaga 900
tccccagatg atgaactgtt atacttacca gtgagggggt gtgagactta tgaatgctg 960
ttgaagatca aagagtcctt ggaactcatg cagtaccttc ctacgcacac aattgaaacg 1020
tacaggcaac agcaacagca gcagcaccag cacttacttc agaaacagac ctcaatacag 1080
tctccatctt catatggtaa cagctcccca cctctgaaca aaatgaacag catgaacaag 1140
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attcctgatg gcatgggagc caacattccc atgatgggca cccacatgcc aatgggtgga 1260
gacatgaatg gactcagccc caccaggcca ctccctcccc cactctccat gccatccacc 1320
tccactgca cacccccacc tccgtatccc acagattgca gcattgtcag gatctggcaa 1380
gtctga 1386

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<210> 337

<211> 1551

<212> DNA

<213> Homo sapiens

<400> 337

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ccatcagaag atggtgagac aaacaagatt gagattagca tggactgtat ccgcatgcag 180
gactcgggac tgagtgaacc catgtggcca cagtagacga acctggggct cctgaacgcg 240
atggaccagc agattcagaa cggctcctcg tccaccagtc cctataacac agaccacgcg 300
cagaacagcg tcacggcgcc ctgcacctac gcacagccca gctccacctt cgatgctctc 360
tctccatcac ccgccatccc ctccaacacc gactaccag gcccgcacag tttcgacgtg 420
tccttcagc agtcgagcac cgccaagtgc gccacctgga cgtattccac tgaactgaag 480
aaactctact gccaaattgc aaagacatgc cccatccaga tcaagggtgat gacccacct 540
cctcagggag ctgttatccg cgccatgct gtctacaaaa aagctgagca cgtcacggag 600
gtgggtgaagc ggtgccccaa ccatgagctg agccgtgaat tcaacgaggg acagattgcc 660
cctcctagtc atttgattcg agtagagggg aacagccatg cccagtatgt agaagatccc 720

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atcacaggaa gacagagtgt gctggtacct tatgagccac cccaggttgg cactgaattc 780
acgacagtct tgtacaattt catgtgtaac agcagttgtg ttggagggat gaaccgccgt 840
ccaattttta tcatgtgtac tctggaaacc agagatgggc aagtcctggg ccgacgctgc 900
tttgaggccc ggatctgtgc ttgccaggga agagacagga aggcggatga agatagcatc 960
agaaagcagc aagtttcgga cagtacaaag aacggtgatg gtacgaagcg cccgtttcgt 1020
cagaacacac atggtatcca gatgacatcc atcaagaaac gaagatcccc agatgatgaa 1080
ctgttatact taccagttag gggccgtgag acttatgaaa tgctgttgaa gatcaaagag 1140
tccctggaac tcatgcagta ccttcctcag cacacaattg aaacgtacag gcaacagcaa 1200
cagcagcagc accagcactt acttcagaaa cagacctcaa tacagtctcc atcttcatat 1260
ggtaacagct cccacactct gaacaaaatg aacagcatga acaagctgcc ttctgtgagc 1320
cagcttatca accctcagca ggcgaacgcc ctcaactcta caaccattcc tgatggcatg 1380
ggagccaaca tcccatgat gggcacccac atgccaatgg ctggagacat gaatggactc 1440
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<210> 338

<211> 586

<212> PRT

<213> Homo sapiens

<400> 338

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Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
      5                                10                        15

Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Arg Asn
      20                                25                        30

Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
      35                                40                        45

Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Pro Thr Phe Asp Ala
      50                                55                        60

Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
      65                                70                        75                        80

His Ser Ser Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
      85                                90                        95

Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
      100                               105                        110

Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
      115                               120                        125

Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
      130                               135                        140

Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
      145                               150                        155                        160

Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn
      165                               170                        175

Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val

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180					185					190					
Leu	Val	Pro	Tyr	Glu	Pro	Pro	Gln	Val	Gly	Thr	Glu	Phe	Thr	Thr	Val
	195						200					205			
Leu	Tyr	Asn	Phe	Met	Cys	Asn	Ser	Ser	Cys	Val	Gly	Gly	Met	Asn	Arg
	210					215					220				
Arg	Pro	Ile	Leu	Ile	Ile	Val	Thr	Leu	Glu	Thr	Arg	Asp	Gly	Gln	Val
	225					230					235				240
Leu	Gly	Arg	Arg	Cys	Phe	Glu	Ala	Arg	Ile	Cys	Ala	Cys	Pro	Gly	Arg
				245					250					255	
Asp	Arg	Lys	Ala	Asp	Glu	Asp	Ser	Ile	Arg	Lys	Gln	Gln	Val	Ser	Asp
			260					265					270		
Ser	Thr	Lys	Asn	Gly	Asp	Gly	Thr	Lys	Arg	Pro	Phe	Arg	Gln	Asn	Thr
	275						280					285			
His	Gly	Ile	Gln	Met	Thr	Ser	Ile	Lys	Lys	Arg	Arg	Ser	Pro	Asp	Asp
	290					295					300				
Glu	Leu	Leu	Tyr	Leu	Pro	Val	Arg	Gly	Arg	Glu	Thr	Tyr	Glu	Met	Leu
	305					310					315				320
Leu	Lys	Ile	Lys	Glu	Ser	Leu	Glu	Leu	Met	Gln	Tyr	Leu	Pro	Gln	His
				325					330					335	
Thr	Ile	Glu	Thr	Tyr	Arg	Gln	Gln	Gln	Gln	Gln	Gln	His	Gln	His	Leu
			340					345					350		
Leu	Gln	Lys	Gln	Thr	Ser	Ile	Gln	Ser	Pro	Ser	Ser	Tyr	Gly	Asn	Ser
	355						360					365			
Ser	Pro	Pro	Leu	Asn	Lys	Met	Asn	Ser	Met	Asn	Lys	Leu	Pro	Ser	Val
	370					375					380				
Ser	Gln	Leu	Ile	Asn	Pro	Gln	Gln	Arg	Asn	Ala	Leu	Thr	Pro	Thr	Thr
	385					390					395				400
Ile	Pro	Asp	Gly	Met	Gly	Ala	Asn	Ile	Pro	Met	Met	Gly	Thr	His	Met
				405					410					415	
Pro	Met	Ala	Gly	Asp	Met	Asn	Gly	Leu	Ser	Pro	Thr	Gln	Ala	Leu	Pro
			420					425					430		
Pro	Pro	Leu	Ser	Met	Pro	Ser	Thr	Ser	His	Cys	Thr	Pro	Pro	Pro	Pro
	435						440					445			
Tyr	Pro	Thr	Asp	Cys	Ser	Ile	Val	Ser	Phe	Leu	Ala	Arg	Leu	Gly	Cys
	450					455					460				
Ser	Ser	Cys	Leu	Asp	Tyr	Phe	Thr	Thr	Gln	Gly	Leu	Thr	Thr	Ile	Tyr
	465					470					475				480

Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro
 485 490 495

Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln
 500 505 510

Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser
 515 520 525

Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val
 530 535 540

Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro
 545 550 555 560

Arg Asp Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn
 565 570 575

Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu
 580 585

<210> 339

<211> 641

<212> PRT

<213> Homo sapiens

<400> 339

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
 5 10 15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
 20 25 30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
 35 40 45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
 50 55 60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
 65 70 75 80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
 85 90 95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
 100 105 110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
 115 120 125

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
 130 135 140

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
 145 150 155 160
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
 165 170 175
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
 180 185 190
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
 195 200 205
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
 210 215 220
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
 225 230 235 240
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
 245 250 255
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
 290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
 370 375 380
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser
 405 410 415
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser
 420 425 430
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg

435 440 445
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile
 450 455 460
 Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu
 465 470 475 480
 Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser
 485 490 495
 His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly
 500 505 510
 Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr
 515 520 525
 Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp
 530 535 540
 Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys
 545 550 555 560
 Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His
 565 570 575
 Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser
 580 585 590
 Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg
 595 600 605
 Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe
 610 615 620
 Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly
 625 630 635 640

Glu

<210> 340

<211> 448

<212> PRT

<213> Homo sapiens

<400> 340

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
 5 10 15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
 20 25 30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
 35 40 45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
 50 55 60
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
 65 70 75 80
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
 85 90 95
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
 100 105 110
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
 115 120 125
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
 130 135 140
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
 145 150 155 160
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
 165 170 175
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
 180 185 190
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
 195 200 205
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
 210 215 220
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
 225 230 235 240
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
 245 250 255
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
 290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335

Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
 370 375 380
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
 Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys
 405 410 415
 Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser
 420 425 430
 Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro
 435 440 445
 <210> 341
 <211> 356
 <212> PRT
 <213> Homo sapiens
 <400> 341
 Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
 5 10 15
 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn
 20 25 30
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
 35 40 45
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
 50 55 60
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65 70 75 80
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
 85 90 95
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
 100 105 110
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
 115 120 125
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
 130 135 140
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn

145 150 155 160
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn
 165 170 175
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val
 180 185 190
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val
 195 200 205
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg
 210 215 220
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val
 225 230 235 240
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg
 245 250 255
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp
 260 265 270
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Ser Arg Gln Asn Thr
 275 280 285
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp
 290 295 300
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu
 305 310 315 320
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His
 325 330 335
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu
 340 345 350
 Leu Gln Lys Gln
 355

 <210> 342
 <211> 680
 <212> PRT
 <213> Homo sapiens

 <400> 342
 Met Asn Phe Glu Thr Ser Arg Cys Ala Thr Leu Gln Tyr Cys Pro Asp
 5 10 15

 Pro Tyr Ile Gln Arg Phe Val Glu Thr Pro Ala His Phe Ser Trp Lys
 20 25 30

 Glu Ser Tyr Tyr Arg Ser Thr Met Ser Gln Ser Thr Gln Thr Asn Glu
 35 40 45

Phe Leu Ser Pro Glu Val Phe Gln His Ile Trp Asp Phe Leu Glu Gln
 50 55 60
 Pro Ile Cys Ser Val Gln Pro Ile Asp Leu Asn Phe Val Asp Glu Pro
 65 70 75 80
 Ser Glu Asp Gly Ala Thr Asn Lys Ile Glu Ile Ser Met Asp Cys Ile
 85 90 95
 Arg Met Gln Asp Ser Asp Leu Ser Asp Pro Met Trp Pro Gln Tyr Thr
 100 105 110
 Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn Gly Ser
 115 120 125
 Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser Val Thr
 130 135 140
 Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala Leu Ser
 145 150 155 160
 Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro His Ser
 165 170 175
 Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala Thr Trp
 180 185 190
 Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala Lys Thr
 195 200 205
 Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly Ala Val
 210 215 220
 Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr Glu Val
 225 230 235 240
 Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn Glu Gly
 245 250 255
 Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn Ser His
 260 265 270
 Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val Leu Val
 275 280 285
 Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val Leu Tyr
 290 295 300
 Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg Arg Pro
 305 310 315 320
 Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val Leu Gly
 325 330 335

Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg Asp Arg
 340 345 350
 Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp Ser Thr
 355 360 365
 Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr His Gly
 370 375 380
 Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp Glu Leu
 385 390 395 400
 Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu Leu Lys
 405 410 415
 Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His Thr Ile
 420 425 430
 Glu Thr Tyr Arg Gln Gln Gln Gln Gln Gln His Gln His Leu Leu Gln
 435 440 445
 Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser Ser Pro
 450 455 460
 Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val Ser Gln
 465 470 475 480
 Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr Ile Pro
 485 490 495
 Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met Pro Met
 500 505 510
 Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro Pro Pro
 515 520 525
 Leu Ser Met Pro Ser Thr Ser Gln Cys Thr Pro Pro Pro Pro Tyr Pro
 530 535 540
 Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys Ser Ser
 545 550 555 560
 Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr Gln Ile
 565 570 575
 Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro Glu Gln
 580 585 590
 Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln Leu His
 595 600 605
 Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser Ala Ser
 610 615 620
 Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val Ile Asp

161

625 630 635 640
 Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro Arg Asp
 645 650 655
 Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn Lys Gln
 660 665 670
 Gln Arg Ile Lys Glu Glu Gly Glu
 675 680

 <210> 343
 <211> 461
 <212> PRT
 <213> Homo sapiens

 <400> 343
 Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
 5 10 15
 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn
 20 25 30
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
 35 40 45
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
 50 55 60
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65 70 75 80
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
 85 90 95
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
 100 105 110
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
 115 120 125
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
 130 135 140
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
 145 150 155 160
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn
 165 170 175
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val
 180 185 190
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val
 195 200 205

Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg
 210 215 220
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val
 225 230 235 240
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg
 245 250 255
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp
 260 265 270
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr
 275 280 285
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp
 290 295 300
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu
 305 310 315 320
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His
 325 330 335
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln Gln His Gln His Leu
 340 345 350
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser
 355 360 365
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val
 370 375 380
 Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr
 385 390 395 400
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met
 405 410 415
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro
 420 425 430
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro
 435 440 445
 Tyr Pro Thr Asp Cys Ser Ile Val Arg Ile Trp Gln Val
 450 455 460

<210> 344

<211> 516

<212> PRT

<213> Homo sapiens

<400> 344

290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
 370 375 380
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
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LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ,
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FAN, Liqun [CN/US]; 14116 SE 46th Street, Bellevue,
WA 98006 (US).

(54) Title: COMPOUNDS AND METHODS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER

(57) Abstract: Compounds and methods for the treatment and diagnosis of lung cancer are provided. The inventive compounds include polypeptides containing at least a portion of a lung tumor protein. Vaccines and pharmaceutical compositions for immunotherapy of lung cancer comprising such polypeptides, or DNA molecules encoding such polypeptides, are also provided, together with DNA molecules for preparing the inventive polypeptides.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/08896

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/47 C12N15/12 C12N15/10 C12N15/62 C07K16/30
G01N33/53 C12N15/11 C12Q1/68 A61K39/395 A61K38/17
A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BRASS N ET AL: "Translation initiation factor eIF-4gamma is encoded by an amplified gene and induces an immune response in squamous cell lung carcinoma" HUMAN MOLECULAR GENETICS, GB, OXFORD UNIVERSITY PRESS, SURREY, vol. 6, no. 1, January 1997 (1997-01), pages 33-39, XP002112603 ISSN: 0964-6906 the whole document --- -/--	1,11,17, 18,21, 22,29, 40-53

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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- "O" document referring to an oral disclosure, use, exhibition or other means
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- "&" document member of the same patent family

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/08896

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BALDI A ET AL: "DIFFERENTIAL EXPRESSION OF RB2/P130 AND P107 IN NORMAL HUMAN TISSUES AND IN PRIMARY LUNG CANCER" CLINICAL CANCER RESEARCH,US,THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, vol. 3, no. 10, October 1997 (1997-10), pages 1691-1697, XP002910343 ISSN: 1078-0432 the whole document	1,11, 40-47, 54,56,57
X	WO 98 35985 A (ELECTROPHORETICS INTERNATIONAL ;HANASH SAMIR M (US)) 20 August 1998 (1998-08-20) the whole document	1,11,17, 21,54,57
X	WO 96 30389 A (MILLENNIUM PHARM INC) 3 October 1996 (1996-10-03) the whole document page 10, line 15 -page 12, line 10	1,9-11, 17,18, 40-60
X	DATABASE EMBL NUCLEOTIDE AND PROTEIN SEQUENCES,17 March 1999 (1999-03-17), XP002149009 HINXTON, GB AC = AI468638. Soares_NhHMPu S1 Homo sapiens cDNA clone IMAGE:2125318 3', mRNA sequence. EST. abstract	1,2,5-8, 58,59
X	DATABASE EMBL NUCLEOTIDE AND PROTEIN SEQUENCES,18 April 1997 (1997-04-18), XP002149010 HINXTON, GB AC = AA340797. EST46165 Fetal kidney II Homo sapiens cDNA 3' end, mRNA sequence. EST. abstract	1,2,5-8, 58,59
X	EP 0 695 760 A (HOFFMANN LA ROCHE) 7 February 1996 (1996-02-07) the whole document	1,9-11, 18, 40-47, 54-57
X	WO 94 06929 A (MERCK PATENT GMBH ;STAHEL ROLF (CH)) 31 March 1994 (1994-03-31) abstract page 2, line 6-32 page 3, line 5-14	1,11,54, 57

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/08896

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 96 28473 A (MEDENICA RAJKO D) 19 September 1996 (1996-09-19)</p> <p>abstract page 2, line 15 -page 3, line 18 page 4, line 1-30</p> <p>---</p>	<p>1,11,17, 18,21, 22,35-47</p>
X	<p>WO 98 46788 A (KUFR PETER ;MICROMET GMBH (DE); ZIPPELIUS ALFRED (DE)) 22 October 1998 (1998-10-22)</p> <p>abstract page 1-10; examples 1-4,6</p> <p>---</p>	<p>1,18, 48-53, 58-60</p>
X	<p>WO 95 21862 A (BRIGHAM & WOMENS HOSPITAL) 17 August 1995 (1995-08-17)</p> <p>page 3, paragraph 2 -page 5, paragraph 4 page 10-41</p> <p>---</p>	<p>1,9-12, 17,18, 22,25, 35-39, 51,52, 58-60</p>
X	<p>WO 97 07244 A (US GOVERNMENT) 27 February 1997 (1997-02-27)</p> <p>the whole document</p> <p>---</p>	<p>1</p>
X	<p>MARSHALL A AND HODGSON J: "DNAchips: an array of possibilities" NATURE BIOTECHNOLOGY, vol. 16, January 1998 (1998-01), pages 27-31, XP002917754 the whole document</p> <p>---</p>	<p>1</p>
X	<p>RAMSEY GRAHAM: "DNA chips: state of the art" NATURE BIOTECHNOLOGY, vol. 16, January 1998 (1998-01), pages 40-44, XP002917751 the whole document</p> <p>---</p>	<p>1</p>
A	<p>WO 91 18926 A (FORSGREN ARNE) 12 December 1991 (1991-12-12) cited in the application page 5, line 22-35</p> <p>---</p>	<p>14,25</p>
	<p>---</p> <p>-/--</p>	

INTERNATIONAL SEARCH REPORT

International Application No	PCT/US 00/08896
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>LELIEVRE D ET AL: "STRUCTURAL PROPERTIES OF CHIMERIC PEPTIDES CONTAINING A T-CELL EPITOPE LINKED TO A FUSION PEPTIDE AND THEIR IMPORTANCE FOR IN VIVOINDUCTION OF CYTOTOXIC T-CELL RESPONSES" EUROPEAN JOURNAL OF BIOCHEMISTRY, BERLIN, DE, vol. 249, no. 3, 1997, pages 895-904, XP000929575 ISSN: 0014-2956 the whole document</p> <p style="text-align: center;">---</p>	12,14,25
A	<p>HOGAN KEVIN T ET AL: "The peptide recognized by HLA-A68.2-restricted, squamous cell carcinoma of the lung-specific cytotoxic T lymphocytes is derived from a mutated elongation factor 2 gene." CANCER RESEARCH, vol. 58, no. 22, 15 November 1998 (1998-11-15), pages 5144-5150, XP000946579 ISSN: 0008-5472 the whole document</p> <p style="text-align: center;">---</p>	14,25
A	<p>VISSEREN M J W ET AL: "IDENTIFICATION OF HLA-A 0201-RESTRICTED CTL EPITOPES ENCODED BY THE TUMOR-SPECIFIC MAGE-2 GENE PRODUCT" INTERNATIONAL JOURNAL OF CANCER, NEW YORK, NY, US, vol. 73, no. 1, 1997, pages 125-130, XP000914539 ISSN: 0020-7136 the whole document</p> <p style="text-align: center;">---</p>	14,25
P,X	<p>WO 99 47674 A (CORIXA CORP) 23 September 1999 (1999-09-23) cited in the application SEQ.ID.N.1 page 1, last paragraph -page 32, paragraph 1</p> <p style="text-align: center;">---</p>	1-60
P,X	<p>WO 99 38973 A (CORIXA CORP) 5 August 1999 (1999-08-05) page 1, line 28 -page 4, line 15 page 16, line 12 -page 17, line 10 page 18, line 14 -page 34, line 15</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	1-60

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/08896

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>WANG TONGTONG ET AL: "Identification of genes differentially over-expressed in lung squamous cell carcinoma using combination of cDNA subtraction and microarray analysis." ONCOGENE, vol. 19, no. 12, 16 March 2000 (2000-03-16), pages 1519-1528, XP000951444 ISSN: 0950-9232 the whole document</p>	1-60
T	<p style="text-align: center;">---</p> <p>HENDERSON R A ET AL: "Identification of lung tumor antigens for cancer immunotherapy: Immunological and molecular approaches." IMMUNOLOGICAL INVESTIGATIONS, vol. 29, no. 2, May 2000 (2000-05), pages 87-91, XP000951456 Fourteenth International Convocation on Immunology;Buffalo, New York, USA; October 08-11, 1999 ISSN: 0882-0139 the whole document</p> <p style="text-align: center;">-----</p>	1-60

INTERNATIONAL SEARCH REPORT

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-60 all partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: Invention 1 : Claims 1-60 all partially.

An isolated polypeptide, comprising at least an immunogenic portion of a lung tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence as recited in SEQ.ID.N.1 (a) or sequences that hybridize to SEQ.ID.N.1 (b) and the complements of sequences of (a) or (b); as well as an expression vector, a host cell, an antibody, a fusion protein, a pharmaceutical composition, a vaccine, oligonucleotides and diagnostic kits thereof.

2. Claims: Inventions 2 to 130 : Claims 1-60, all partially.

Same as invention 1, but according to each single sequence as recited in claim 1

(SEQ.ID.N.1-3,6-8,10-13,15-27,29,30,32,34-49,51,52,54,55,57-59,61-69,71,73,74,77,78,80-82,84,86-96,107-109,111,113,125,127-129,131-133,142,144,148-151,153,154,157,158,160,167,168,171,173,175,179,182,184-186,188-191,193,194,198-207,209,210,213,214,217,220-224,253,254-258,260,262-264,270,272,275,276,279-281,286,287,291,293,295,296,300,302,308-310,313,315-317,323,345,347 and 349)

and as recited in claim 3

(SEQ.ID.N.110,112,114,152,155,156,159,161,165,166,169,170,172,174,176,226-252,346,348 and 350)

starting from the second in the list: SEQ.ID.N.2 and following with SEQ.ID.N.3, SEQ.ID.N.6, etc... and ending with SEQ.ID.N.350.

and with the provision that sequences tht belong to the same antigen has been counted as one invention (see below)

3. Claims: Inventions 131-258 : Claims 25-61 all partially

A vaccine comprising an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a lung tumor protein wherein the protein compises an aminoacid sequence encoded by a polynucleotide sequence as recited in claim 25

(SEQ.ID.N.4,5,9,14,28,31,33,50,53,56,60,70,72,75,76,79,83,85,97-106,115-124,126,130,134-141,143,145-147,162-164,177,178,180,181,183,187,192,195-197,208,211,212,215,216,218,219,255-259,261,265-269,271,273,274,277,278,282-285,288-290,292,294,297-299,301,303-307,311,312,314,319-322 and 324-337) and kits for diagnostic thereof.

Same as invention 130, but according to each single sequence as recited in claim 25 and not included in claim 1, starting from the SEQ.ID.N.4 and following with SEQ.ID.N.5, SEQ.ID.N.9, etc... and ending with SEQ.ID.N.337.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

and with the provision that sequences tht belong to the same antigen has been counted as one invention (see below)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 21, 22, 29-31, 34, and 37-39 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Although claim(s) 40-53 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/08896

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